THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—38TH YEAR. SYDNEY, SATURDAY, MAY 26, 1951. No. 21.

Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page.

A Small Outbreak of Acute Benign Lymphocytic Choriomeningitis, by Joyce Parry 745
Syphilis of the Pulmonary Artery, by C. Engel, M.D. 749
Tigloidine as a Substitute for Atropine in the Treatment of Parkinsonism, by E. M. Trautner and C. H. Noack 751
The Use of "Perspex" for Splints, by J. M. Davies, M.B., B.S. 754
Intracranial Abscess following Frontal Sinus Infection, by R. S. Hooper 756
Oligophrenia Phenylpyruvica, or Følling's Disease, by S. J. Cantor, D.P.M. 761
Some Psycho-Physical Aspects of Backache, by E. Haslett Frazer 763

REPORTS OF CASES—

Krukenberg Tumours of Both Ovaries Secondary to Carcinoma of the Stomach, by Philip C. Thomas, M.R.C.O.G. 766

REVIEWS—

Methods in Medical Research 767
An Ancient Chinese Medical Manuscript 767
The Biology of Human Starvation 767
A Year Book of Urology 768

BOOKS RECEIVED 768

LEADING ARTICLES—

Detection of the Unrecognized Diabetic 769

CURRENT COMMENT—

The Importance of Controls 770
Hexachlorophene and the Surgical Scrub 770
Oral and Rectal Temperatures in Man 771

CURRENT COMMENT—Continued. Page.

Diabetic Renal Disease 772
The Management of Severe Gastro-Duodenal Hæmorrhage 773

ABSTRACTS FROM MEDICAL LITERATURE—

Therapeutics 774
Neurology and Psychiatry 774

BRITISH MEDICAL ASSOCIATION NEWS—

Scientific 776

THE ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS—

Allocation of Supplies of Cortisone 778
Sims Commonwealth Travelling Professor, 1951 .. 778
Wunderly Travelling Scholarships 779

POST-GRADUATE WORK—

The Post-Graduate Committee in Medicine in the University of Sydney 779

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 779

CONGRESSES—

International Congress of Physical Medicine (1952) 779

OBITUARY—

Rupert Walter Hornabrook 779

AUSTRALIAN MEDICAL BOARD PROCEEDINGS—

Tasmania 780

NOMINATIONS AND ELECTIONS 780

MEDICAL APPOINTMENTS 780

DIARY FOR THE MONTH 780

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 780

EDITORIAL NOTICES 780

A SMALL OUTBREAK OF ACUTE BENIGN LYMPHOCYTIC CHORIOMENINGITIS.

By JOYCE PARRY,

Registrar, Brisbane Children's Hospital, Brisbane.

ACUTE benign lymphocytic choriomeningitis is defined as a type of meningitis of acute onset, of brief course and favourable outcome, characterized by a predominantly lymphocytic pleocytosis in the cerebro-spinal fluid and by the absence of bacteria (Wallgren).

In the five-week period from August 7 to September 13, 1950, 11 patients suffering from this condition were treated as in-patients of the Brisbane Children's Hospital. Previously an occasional case of aseptic meningitis had occurred, but not a number of cases simultaneously, so that an epidemic may be suspected.

Acute benign lymphocytic choriomeningitis is caused by a virus of medium size which may affect monkeys and mice as well as man. This virus was first isolated by Armstrong and Lillie in 1934. Since then the virus has been recovered from mice in apartment houses in which human cases of the disease have occurred. The virus is readily passed in susceptible mice and guinea-pigs by intracerebral inoculation.

The majority of reported cases are isolated ones, although an epidemic has recently been reported by Wallgren. The 21 cases reviewed by Green *et alii* occurred over a period of ten years.

The virus of lymphocytic choriomeningitis is said to produce three types of clinical manifestations in man: (i) grippal or systemic illness without involvement of the central nervous system; (ii) encephalitis; (iii) meningitis. The first type of illness has been proved only in workers handling the virus, but it is interesting to note that at the time at which our cases occurred an epidemic of so-called "influenza" was raging in Brisbane, and most of the patients gave a history that at least one other member of the family had recently "had the 'flu".

The 11 cases here presented all belong to the third group. Unfortunately we were not able to carry out virus studies on our patients.

Clinical Manifestations.

The clinical findings in the 11 cases are summarized in Table I. The series consists of seven male and four female patients, all white children, the youngest being a breast-fed baby, aged eight weeks, and the oldest a girl, aged nine years. The patients came from different social groups and economic circumstances and from different suburbs of Brisbane, with two exceptions—one patient from the Redcliffe district and one from the Sandgate district, 25 and 20 miles respectively from Brisbane. No two cases occurred in the same household or for that matter in the same or adjoining suburbs. No contact between the cases could be traced. This is in contrast to findings previously reported, in which cases occurring in the same building or in dwellings in the same street are more the rule.

Ten of the children gave a history of excellent previous health. The disease in Case I occurred while the child was being treated in hospital. He was suffering from bronchiectasis and recurrent attacks of bronchitis. The patient in Case X had had an injection for immunization against diphtheria thirteen days previously. None of the other children (except the patient in Case I, who had been receiving intramuscular injections of penicillin for his chest condition) had had injections of any type in the six months preceding the illness.

All the patients except the babies (Cases III and X) had symptoms of malaise and generalized pains in limbs and back.

TABLE I.

Case Number, Patient, Sex, Age.	Duration of Symptoms before Admission to Hospital.	Temperature on Admission to Hospital.	Headache.	Vomiting.	Other Features of History.	Clinical Examination.				Duration of Symptoms and Signs After Admission to to Hospital.	Remarks.
						General Findings.	Throat.	Neck Stiffness.	Back Stiffness.		
I: B.L., M., 3 years.	1 day.	100° F.	Frontal; worse on sitting up.	Present.	In-patient with bronchiectasis and recurrent bronchitis; drowsy.	Râles and rhonchi both lung bases. General abdominal tenderness. Pale. Knee and ankle jerks exaggerated. Superficial abdominal reflexes absent.	No abnormality.	++	+	4 days.	Alert and clinically well in 24 hours. Had been having "Procillin" intramuscularly for chest condition.
II: T.T., M., 4 years.	"Off colour" for 1 week; really ill for 1 day.	101·4° F.	Frontal; chiefly right side, worse on sitting up.	Present.	Tired, listless and fretful for 1 week. Feverish and vomiting for 1 day.	Restless. No loss of movement, but legs rather flaccid. Knee and ankle jerks equal and exaggerated. Superficial abdominal reflexes absent.	Tonsils enlarged with patches of exudate on both.	+	+	Pyrexia for 3 days. In-patient for 5 days.	Slight ataxia present when out of bed on fourth day. Improved on fifth day.
III: J.D., F., 8 weeks.	2 days.	102° F.	?	Present.	Crying when picked up; irritable.	Bulging fontanelle. no other abnormality.	No abnormality.	−	−	3 days.	Breast-fed baby. Mother well.
IV: M.P., F., 9 years.	2 days.	103·2° F.	Occipital; worse on sitting up.	Present.	Confused; delirious; pain in back.	Tachycardia. Knee and ankle jerks equal and exaggerated. Superficial abdominal reflexes absent.	Pharynx very red. Post-nasal pus present.	++	+	4 days. Pyrexia and stiffness for 3 days.	Neck stiffness particularly severe for 3 days.
V: K.S., M., 8 years.	1 day.	102·4° F.	Present.	Present.	Hit on head by stone previous day. No symptoms immediately after injury; dizzy day after injury.	Small hæmatoma of forehead. Knee and ankle jerks equal and exaggerated. Superficial abdominal reflexes present.	No abnormality.	++	+	4 days.	
VI: R.W., M., 18 months.	2 days.	101·4° F.	Present.	Present.	Listless, anorexic, irritable.	Knee and ankle jerks present and exaggerated. Superficial abdominal reflexes absent.	Acute follicular tonsillitis.	+	−	Pyrexia 4 days.	Two days after admission to hospital left ptosis developed; had decreased before patient's discharge from hospital on fifteenth day.
VII: P.B., F., 2½ years.	Influenza 3 weeks previously; had completely recovered. Ill for 3 days before admission.	99·4° F.	Present.	Present.	Listless, drowsy; painful ears.	Right internal strabismus. Knee jerks equal and exaggerated. Ankle clonus. Superficial abdominal reflexes absent.	Pharynx very red.	+	+	Pyrexia 6 days. squint 9 days.	Strabismus not normally present in this child. Gradually decreased and completely disappeared by tenth day. Vomiting persisted — given intravenous therapy to combat dehydration.
VIII: J.L., M., 4½ years.	Had completely recovered after mumps and measles one month before; ill for 1 day preceding admission.	103·6° F.	Present.	Present.	General aches and pains following fall preceding day. Cough, irritable and crying for 1 day.	No evidence of injury after fall. Soft systolic murmur all areas. Knee and ankle jerks exaggerated. Superficial abdominal reflexes absent.	Tonsils enlarged. Throat very inflamed.	+	None on admission to hospital but severe 24 hours later.	4 days.	Symptoms increased in the 24 hours following admission to hospital At this time knee and Ankle jerks were absent. Lumbar puncture showed cerebro-spinal fluid findings changed from preceding specimen (see Table II).
IX: A.K., M., 2½ Years.	2 days.	102·8° F.	?	Present.	Ill 2 days. Vomiting and feverish for 1 day.	Knee and ankle jerks exaggerated. Superficial abdominal reflexes doubtful.	Tonsils enlarged.	++	+	4 days.	Back stiffness persisted for 3 days.

TABLE I.—*Continued.*

Case Number, Patient, Sex, Age.	Duration of Symptoms before Admission to Hospital.	Temperature on Admission to Hospital.	Headache.	Vomiting.	Other Features of History.	Clinical Examination.				Duration of Symptoms and Signs After Admission to to Hospital.	Remarks.
						General Findings.	Throat.	Neck Stiffness.	Back Stiffness.		
X: C.S., M., 9 months.	6 days.	102° F.	?	Present.	Feverish — given by sulphadiazine by private doctor without effect; back stiff, 1 day.	Irritable when touched. Drowsy when alone. Fontanelle and ankle jerks exaggerated. Superficial abdominal reflexes absent.	No abnormality.	+ Slight head retraction present.	+	6 days. Pyrexia 5 days.	Injection of diphtheria toxoid given 13 days before his admission to hospital.
XI: J.T., F., 2 years.	2 days.	102° F.	?	Present.	Fever, vomiting, irritability.	Pale; looked very ill. Head lag. Knee and ankle jerks exaggerated. Superficial abdominal reflexes absent.	Pharynx flamed.	+	+	4 days.	Looked much better in 24 hours.

Vomiting and feverishness were present in all cases. In Case VII vomiting persisted after the child's admission to hospital, and intravenous therapy had to be instituted and was continued for thirty-six hours. The temperature on admission to hospital ranged from 99·4° to 103·6° F., the average being 101·8° F. Fever lasted for from three to six days after admission to hospital, the average being four days, and the temperature fell by lysis in all cases.

Irritability was present in ten cases and the remaining child was drowsy.

The seven older children complained of headache, either occipital or frontal, and in three of these cases the headache was greatly increased by the patient's sitting erect.

Physical examination of the patients on their admission to hospital presented several definite factors common to all cases. There was not the clouding of consciousness associated with purulent meningitis, although ten of the children were irritable. In ten cases the neck and back were stiff and the knee and ankle jerks were exaggerated, and in nine the superficial abdominal reflexes were absent. The exception to these findings was Case III, that of a baby aged eight weeks, who presented no abnormality on physical examination other than a bulging anterior fontanelle. Seven of the children had acute pharyngitis or acute follicular tonsillitis.

In no case was a rash present, nor did any lymph gland enlargement or parotid swelling or tenderness occur. There was no papilœdema and no nystagmus.

Case I, in which the illness occurred while the patient was being treated in the hospital, was at first thought to be a cerebral complication of the bronchiectasis. However, this was discounted by the rapidity with which the child completely recovered; he was well within forty-eight hours.

In Case VI the patient developed left ptosis and a small left pupil two days after his admission to hospital. These rapidly diminished and were much less on the patient's discharge from hospital, and had almost completely disappeared when he was examined four weeks later.

The patient in Case VII presented with a left internal strabismus, which was not normally present in this child, and which had completely disappeared by the tenth day in hospital.

A careful watch was kept on all patients for any signs of muscular weakness or paresis, but except in the two cases mentioned none occurred.

Laboratory Findings.

The laboratory findings in these cases are presented in Table II.

Cerebro-Spinal Fluid.

The findings in the specimen of cerebro-spinal fluid obtained by lumbar puncture in each case are recorded. Lumbar puncture was repeated to allow observation of progress in five cases. Two of these patients had had normal cerebro-spinal fluid on their admission to hospital, but no clinical improvement in twenty-four hours. The fluid obtained at the second puncture in both cases contained an increased number of cells; in one the increase was from 0 to 4000 per cubic millimetre, showing the rapidity with which the cell count in the cerebro-spinal fluid may rise.

The cerebro-spinal fluid was collected in dry, sealed, sterile glass bottles, which had been autoclaved, and the cell count and other laboratory investigations were carried out immediately after collection of the specimen.

The cerebro-spinal fluid cell count appeared unrelated to the degree of temperature. The total cell count varied from 27 to 4500 per cubic millimetre. The type of cell was predominantly lymphocytic, but if lumbar puncture was performed very early in the disease polymorphonuclear leucocytes were in excess, lymphocytes predominating as the disease advanced.

The cerebro-spinal fluid was clear or opalescent and the pressure was increased in two cases. In all cases the sugar content was within normal limits.

In nine cases the amount of protein was estimated in the initial cerebro-spinal fluid specimen, and was normal in all, varying from 20 to 150 milligrammes *per centum*.

Estimation of the cerebro-spinal fluid chloride content was performed only sporadically in our cases, since it appears that little is to be learned from this test. It was within normal limits in each of the five cases in which it was performed.

There were no organisms in smears of the cerebro-spinal fluid in any case, and attempts at culture for bacteria were all unsuccessful.

Blood.

White blood cell counts were made in seven cases, and the numbers and differential counts were normal in three. The remaining four counts all revealed slight to moderate leucocytosis; in three there was an increase in cells of the granular series.

The hæmoglobin value was within normal limits in the six cases in which it was estimated.

TABLE II.
Laboratory Findings.[1]

Case Number.	Date of Lumbar Puncture.	Cerebro-spinal Fluid.						Blood: Total White Cells per Cubic Millimetre.	Paul-Bunnell Test Result.
		Appearance.	Pressure.	Cell Count per Cubic Millimetre and Type of Cell.	Sugar. (Milligrammes *per Centum.*)	Protein. (Milligrammes *per Centum.*)	Chloride. (Milligrammes *per Centum.*)		
I	August 8	Opalescent.	Normal.	800; 60% mononuclear, 40% polymorphonuclear.	45	Not estimated.	Not estimated.	22,000	Negative.
II	August 18	Clear.	135 millimetres.	295; chiefly lymphocytes.	45	20	Not estimated.	Not estimated.	Test not performed.
III	August 18	Clear.	190 millimetres.	230; chiefly polymorphonuclear.	40	30	Not estimated.	9,800	Negative.
IV	August 21	Opalescent.	Normal.	Numerous polymorphonuclear cells.	40	80	660	16,200	Negative.
V	August 9	Turbid.	Normal.	720; chiefly lymphocytes.	35	75	720	Not estimated.	Negative.
	August 16	Clear.	Normal.	140; lymphocytes.	35	60	Not estimated.		
VI	August 8	Turbid.	>300 millimetres.	2000; 70% polymorphonuclear.	45	150	Not estimated.	13,200	Negative.
VII	August 16	Clear.	>200 millimetres.	35; polymorphonuclear.	35	30	740	28,200	Negative.
VIII	August 28	Clear.	120 millimetres.	2.	40	20	Not estimated.	8,100	Negative.
	August 29	Turbid.	Normal.	4000; chiefly polymorphonuclear.	45	100			
IX	September 2	Clear.	Normal.	4500; 50% lymphocytes, 50% polymorphonuclear.	Not estimated.	Not estimated.	Not estimated.	Not estimated.	Negative.
	September 6	Clear.	Normal.	16; lymphocytes.	40	20	710		
X	September 8	Opalescent.	Normal.	670; chiefly polymorphonuclear.	Present.	65	695	Not estimated.	Negative.
	September 11	Clear.	180 millimetres.	70; lymphocytes.	40	50	670		
XI	September 13	Clear.	Normal.	0.	35	20	Not estimated.	9,400	Negative.
	September 14	Clear.	Normal.	27; polymorphonuclear.	20	10	Not estimated.		

[1] In all cases the urine was normal and the cerebro-spinal fluid was sterile.

White cell counts and hæmoglobin estimations were repeated in ten cases three to five weeks after the patient's discharge from hospital. In Case I mild leucocytosis was still present, but in all other cases the results were within normal limits.

Paul-Bunnell tests were performed in three cases before the children left hospital, and gave negative results in all cases. This test has been repeated in ten of the cases three to five weeks after the child's discharge from hospital, and the result was negative in all cases.

Urine.

Urine tests revealed no abnormalities.

Diagnosis and Differential Diagnosis.

The diagnosis of lymphocytic choriomeningitis is based chiefly on the cerebro-spinal fluid findings. The cells are increased in number and there is a predominance of lymphocytes, although polymorphonuclear leucocytes may be in excess in the early stages. Later, however, mononuclear leucocytes constitute about 90% of the total cells. The sugar content is normal and the protein content normal or slightly raised. There is in these patients an absence of otitis, mastoiditis and other infections. There is a rapid improvement in the clinical condition of the patient. The presence of other cases in the same vicinity helps to strengthen the diagnosis.

The exact diagnosis of lymphocytic choriomeningitis may be made on the isolation of the virus from the cerebro-spinal fluid of patients in the acute stage of the disease, and on the demonstration of an increase in the titre of antibody against the virus following the acute illness in question. The presence of antibodies in the serum is apparently not absolutely diagnostic, as Armstrong found them in 11% of people who gave no history of meningitis. In our cases, owing to lack of laboratory facilities for investigation of virus diseases, the diagnosis had to be made clinically.

Non-paralytic cases of poliomyelitis may present a similar clinical picture. However, during the period in question, and the two weeks preceding the onset of the illness in the first case of our series, no cases of paralytic poliomyelitis occurred in the metropolitan area of Brisbane.

Tuberculous meningitis was excluded by the rapid and complete clinical improvement of all the patients.

Mumps meningo-encephalitis may lead to difficulties in diagnosis. In Cases IV and V of the present series there was a history of a severe attack of mumps several years previously, and another patient (Case VII) had had mumps about one month before his admission to hospital with benign lymphocytic choriomeningitis. He had, however, been symptomless for three weeks before his admission. None of the other children had ever had mumps, and none could give a history of recent contact with mumps.

Infective mononucleosis may give rise to a variety of meningitic and encephalitic signs. Tidy emphasizes that every published case of lymphocytic choriomeningitis may in reality be a case of glandular fever. In none of the 11 cases here presented were the physical findings or blood picture suggestive, and agglutination tests gave negative results in all cases.

Coxsackie virus infections have recetly been shown to give rise to symptoms similar to those occurring in the cases here presented. Findlay and Howard report cases of Bornholm disease complicated by lymphocytic meningitis, with complement-fixing antibodies against Coxsackie virus II in the blood. In favour of the diagnosis of Coxsackie virus infection is the relative frequency of poly-

morphonuclear leucocytes occurring in the cerebro-spinal fluid, the occurrence of sore throat and the short duration of the illness.

In view of recent studies emphasizing the possibility of paralytic poliomyelitis occurring in recently immunized children, Case X seems worthy of comment. Stellerman has reported the case of a nurse suffering from aseptic meningitis after immunization with diphtheria toxoid. None of the other ten children in our series had had any recent immunization.

Clinical Course and Management.

In 10 of the 11 cases the course of the disease has been short, self-limited and benign, in that there were no deaths and no residual signs or symptoms. The remaining patient had mild ptosis, which had greatly decreased on the child's discharge from hospital.

The duration of symptoms varied from two to sixteen days. The stay in hospital varied from five to nineteen days, the average being eight or nine days.

Ten of the patients have been followed up and examined four to six weeks after their discharge from hospital. They are all well and have no after-effects. The ptosis in Case VI is now only slight.

The treatment is entirely symptomatic, and consists of complete bed rest with analgesics and fluid and diet control depending on the requirements of the individual patient. If vomiting persists and is severe, intravenous alimentation is necessary.

Penicillin and streptomycin were given by intramuscular injection in the earlier cases, but no antibiotics were given in the later ones.

No patient was given any intrathecal medication.

Summary.

1. Eleven cases of benign choriomeningitis are presented. All cases occurred in a five-week period amongst white children, whose ages varied from eight weeks to nine years.

2. The clinical history consisted of headache, vomiting, irritability, fever and general malaise. On examination neck and back stiffness predominated, with absent superficial abdominal reflexes and exaggerated knee and ankle jerks. Acute pharyngitis or tonsillitis occurred in seven patients.

3. Cerebro-spinal fluid changes consisted of an increase in cells varying from 27 to 4500 per cubic millimetre, polymorphonuclear cells often predominating in the early stages, and later in the illness mononuclear cells being in excess. However, mononuclear cells may constitute the majority of cells even in the early stages. The protein content was normal or slightly raised. Other cerebro-spinal fluid findings were normal.

4. Difficulties of diagnosis are mentioned, especially from mumps meningo-encephalitis, glandular fever, preparalytic poliomyelitis and Coxsackie virus infections.

5. Treatment is entirely symptomatic, and consists of general nursing and attention to the requirements of the individual patient.

6. The clinical course in all cases was rapid and favourable. None of the patients died, and in one case mild ptosis is rapidly diminishing. None of the other patients has suffered any after effects.

Acknowledgements.

I wish to thank the medical superintendent and members of the visiting staff of the Brisbane Children's Hospital for permission to publish these cases; Dr. E. H. Derrick, Deputy Director of the Queensland Institute of Medical Research, for information on the recent knowledge of Coxsackie and other virus infections; and the staff of the pathology department, Brisbane Hospital, for carrying out the laboratory investigations. I should also like to extend my grateful thanks to Dr. T. R. Biggs, visiting physician to the Brisbane Children's Hospital, for his helpful advice and assistance in preparing this paper.

References.

Dalldorf, G., Jungeblut, C. W., and Umphlet, M. D. (1946), "Multiple Cases of Coriomeningitis in an Apartment Harbouring Infected Mice", *The Journal of the American Medical Association*, Volume CXXXI, page 25.

Findlay, G. M., and Howard, E. M. (1950), "Coxsackie Viruses and Bornholm Disease", *British Medical Journal*, Volume I, page 1233.

Ford, F. R. (1946), "Acute Benign Lymphocytic Meningitis", in "Diseases of the Nervous System in Infancy, Childhood, and Adolescence", Second Edition, page 512.

Green, W. R., Sweet, L., and Pritchard, R. W. (1949), "Acute Lymphocytic Choriomeningitis. A Study of Twenty-One Cases", *The Journal of Pediatrics*, Volume XXXV, page 688.

Stellerman, H. B. (1948), "Aseptic Meningitis following Immunisation with Diphtheria Toxoid", *American Journal of Diseases of Children*, Volume LXXVI, page 331.

Tidy, H. L. (1946), "Relationship of Benign Lymphocytic Choriomeningitis and Glandular Fever", *The Lancet*, Volume II, page 819.

Wallgren, A. (1949), "An Epidemic of Acute Benign Meningitis", *American Journal of Diseases of Children*, Abstracts, Volume LXXVIII, page 951. Original article: Palmen, Kurt, and Quarna, Kuno (1946), *Svenska lakärtidningen*, Volume XLIII, page 278.

Addendum.

Since this article has been prepared, 17 more patients suffering from acute benign choriomeningitis have been admitted to the Children's Hospital, Brisbane. All children had similar clinical histories and cerebro-spinal fluid findings to those recorded above. All recovered, and to date there have been no sequelæ.

SYPHILIS OF THE PULMONARY ARTERY.

By C. ENGEL, M.D. (Budapest),
Sydney.

SYPHILITIC ARTERITIS affecting the pulmonary artery is an extremely uncommon disease. (In this paper I intend to deal only with disease of the main trunk.) This statement refers to alterations found exclusively in the pulmonary artery and to aneurysms developed in consequence, as well as to those changes which accompany similar findings in the aorta. Publications on the topic are scarce. The total number of cases of this kind reported in the literature hardly amounts to a couple of hundred. On the other hand, it is well known that aortitis is far the most frequent syphilitic disease of the tertiary stage, and even at the present time many thousands succumb to it every year.

Even large and well-frequented clinics and hospitals do not for years on end see one patient suffering from aneurysm of the pulmonary artery. By contrast, in Australia 206 persons die from aneurysm of the aorta every year according to official statistics (1947). In reality this number must be much higher, at least double or treble. To illustrate the rarity of syphilis of the pulmonary artery, let me quote some data from the literature. In Karsner's paper (1933) on productive cicatricial syphilitic disease of the pulmonary artery one may read as follows: "Eleven cases anatomically proved by resonably liberal interpretation are now on record." (In quoting this paper, I would mention that gummatous alterations occur proportionately more often in the pulmonary artery than in the aorta —Herxheimer, 1931.) Groedel (1939) has estimated as in the range 1:250 the ratio of aneurysms of the pulmonary artery to those of the aorta. Deterling and Claget (1947) gave the following figures (obtained from the necropsies at the Mayo Clinic): there occurs one aortic aneurysm in every 140 necropsies, and one of the pulmonary artery in every 17,545 necropsies. But at the same time they report that only about one-third of these aneurysms are probably of syphilitic origin. Accordingly the ratio between these two diseases of syphilitic origin would be approximately 1:370. But there are statistics in which the ratio is even much higher. In the paper of Boyd and Gawack (1939) we read as follows: "No example of aneurysm of the

pulmonary artery has been observed among 1671 cases of aneurysms collected by three authors."[1]

I myself have encountered only one case of syphilitic arteritis affecting the pulmonary artery—and that was more than twenty years ago—in spite of having searched for this condition with avid eagerness for thirty years on a large clinical and post-mortem material.

The subject was a man, aged over fifty years, suffering from liver cirrhosis, with immense ascites requiring frequent aspiration. There was no abuse of alcohol in the anamnesis. The Wassermann reaction of the blood was "+++". Post-mortem examination revealed cirrhosis of the liver and well extended, well advanced typical syphilitic changes on the intima of the pulmonary artery. Only scattered small similar patches could be found in the aorta.

Unfortunately, the case was not complete, as a histological examination was not performed, and so microscopic confirmation of the syphilitic origin was not obtained. For this reason I did not publish the case at that time.

What can be the cause of such a peculiarly striking difference in reaction towards syphilis of two arteries, both of about the same diameter and lying close to each other? The question is of more interest because almost all other pathological alterations of the aortic intima and media occur in the pulmonary artery, though in less frequency and degree, except perhaps atherosclerosis, which is exceedingly common in the pulmonary artery (White, 1937). In most published work the question is hardly dealt with or even mentioned. Obviously authors do not like to raise questions they cannot answer.

Let us try to discuss some details which may be of interest and eventually of value in approaching the problem.

The origin of both vessels is the same, as both developed from the primary arterial tube (*truncus arteriosus*) by its division or rather by the development of the *septum spirale aortico-pulmonale*. Both are approximately, I repeat, of the same diameter; the relation of both to other organs in the anterior mediastinum is about the same. The lymphatics of both run in the same direction. What is the difference between them?

The wall of the aorta is much thicker than that of the *arteria pulmonalis*. Some authors emphasize even that the wall of the pulmonary artery is surprisingly thin for its diameter, almost like that of veins. The difference in the thickness of the wall has a bearing principally on the layer of the *tunica media*, which otherwise has about the same structure, both being of the elastic type. It is well known that in this type of artery the thickness of the layer of elastic fibres is proportional to the blood pressure in the artery. The aorta is conveying arterial blood, the pulmonary artery venous blood. The blood pressure in the aorta is much higher than in the pulmonary artery (about 150 millimetres and 20 millimetres of mercury respectively). The number of *vasa vasorum* is larger in the aorta; this is an important point. The supravalvular part of the *aorta ascendens*, one or two inches above the valves, seems to be the richest in *vasa vasorum*—that is, in just the region where syphilitic lesions on the intima and in the media are to be found with the greatest frequency and intensity.

Can one or the sum of all these differences be of crucial importance? Some authors think so. There is hardly any doubt that the spirochætes invading the walls of both big arteries arrive with the blood-stream via *vasa vasorum*. This happens early in the general dissemination of the spirochætes (spirochætæmia) after they have penetrated the lymphatic barrier. To my mind the supposition of some authors that the spirochætes enter the aorta wall from the lymph glands of the mediastinum by retrograde flow of the lymph (Maitland, 1930) cannot be proved and is not probable at all; I myself do not see the least chance for such a happening.

With the larger number of *vasa vasorum* a bigger mass of spirochætes may enter the wall of the aorta than the wall of the pulmonary artery. The spirochætes which have passed the capillaries of the aortic wall may furthermore find more accommodation to settle down and lodge in the much more abundant perivascular spaces of the aortic wall than in those of the pulmonary artery. There are pathologists who are of the opinion that the larger number of *vasa vasorum* may be considered an important contribution towards explaining why syphilitic lesions are mostly located on the supravalvular area of the aortic intima. According to Saphir and Scott (1930), "the frequency with which syphilis attacks the root of the aorta is due to the rich supply of *vasa vasorum* in this region". Could it not be advocated that this might also be the clue to the different frequency of syphilitic alteration of the two vessels? According to some authors the answer in this regard is in the affirmative. When about two decades ago I interviewed a couple of outstanding pathologists in Hungary on this matter, the opinion of one of them was that the different supply of *vasa vasorum* should be regarded as the main, even the crucial, factor. I myself am not convinced that this difference in supply of *vasa vasorum* is of such decisive importance, even if I do not deprecate its significance. To my mind the different supply of *vasa vasorum* may be well over-compensated by the fact that the initial brunt of spirochætes is borne more by the wall of the pulmonary artery than by the aorta, as the spirochætes enter the circulation by way of the venous blood through the lymphatic barrier. The relative spirochæte content is furthermore always larger in the blood of the pulmonary artery, because the blood passing the wide area of the pulmonary capillaries always deposits a large number of spirochætes in the widely extended perivascular spaces of the lungs. Obviously it may be of much less importance that the spirochætes, as strictly anaerobic, may find more suitable conditions for settling in the wall of the pulmonary artery, conveying venous blood, than in that of the aorta. This possibility is, of course, only apparent, as the wall of the pulmonary artery receives its nutrition via the *vasa vasorum*, which convey arterial blood. One more factor in the field of the *vasa vasorum* must be mentioned. The *vasa vasorum* penetrate the wall of the different arteries to a different depth. In the smaller arteries—for example, those of the muscular type—the *vasa vasorum* split up in the adventitia. In the wall of the aorta they penetrate well into the deeper layers of the media almost to the intima. In the pulmonary artery they do not penetrate so far, they merely enter the outer layers of the media. However, I have found no very detailed investigations on this matter, which to me is regrettable as this difference may be one of the major factors contributing to the different behaviour of the arteries towards syphilis. Some authors are of the opinion that one fact may play a role in the typical localization of syphilitic alterations on a circumscribed place in the ascending aorta, and that is that the impact of the onrushing blood on the aorta wall strikes that area hardest where the syphilitic lesions occur most frequently (Benecke, 1919). Because of the much lower blood pressure this impact is obviously less strong in the pulmonary artery. According to the general consensus of opinion, dynamic factors are well credited with the provoking of syphilitic alterations. There are many examples to support this supposition. Gummas may develop at the place of bone fractures and on such places of the skin as are exposed to slight irritations. This is the reason why gummas are often found on the forehead of Mohammedans, who during their daily prayers often touch the ground with their foreheads.

To summarize, there is a host of dynamic factors which have to be taken into consideration in interpreting the difference in syphilitic involvement of the two arteries. There is no doubt that any one of them or all of them together may contribute to the different behaviour of the two big arteries towards syphilis. But I am far from convinced that these dynamic activities are the decisive factors or the only ones.

I myself regard the presence of a chemical factor as the most important contribution. I hasten to remark that I have no positive proofs for this statement, and to add that it is of course not my idea—similar reasoning can be

[1] An aneurysm of the pulmonary artery shown by G. Hall at a meeting of the New South Wales Branch of the British Medical Association on October 19, 1950, at Saint Vincent's Hospital, Sydney, and well verified *in vivo* by angiography, was not of syphilitic origin.

found in many papers in the literature; in this regard the article by Rosahn (1948) is very interesting. The experience of the last half-century has taught the clinicians to be always and to the highest degree "chemistry-conscious", and the demands of the future are imperative. It is one of the most significant activities in the study of the biology of all pathogenic and non-pathogenic microbes, bacteria and viruses equally to find the most suitable culture medium and to search for the possibility of growth-promoting and of growth-prohibiting factors. Should not similar considerations be remembered in the study of the behaviour of the pathogenic agents in the human organism too?

It seems to me that we cannot help supposing the decisive factor to be a chemical one. Dynamic factors are totally different in the two favourite sites of late syphilis in man, the aorta and the central nervous system, and yet that is where syphilitic involvement of the tertiary stage is most frequent. The following words are often quoted (Beermann *et alii*, 1950): "It requires several thousand spirochætes to infect a mouse, yet only one spirochæta infects a rabbit. In man no tissue is immune against syphilis; in the mouse all tissues are non-reactive; in the rabbit only the testes, the eyes, the skin and the bone react with lesions."

There are innumerable unsolved laboratory and clinical problems in human syphilis; they will not be solved until the searchlight of chemistry makes the hitherto completely obscure field clear. The composition of the interstitial fluid is undoubtedly different in the different organs; there must be some infinitely slight alteration originating from metabolism products of the cells of the organ involved which makes all the difference.

Conclusion.

So I cannot solve the mystery of syphilis of the pulmonary artery; it remains one of the many "unknowns" of human syphilis.

I emphasized in the introduction that syphilis of the pulmonary artery is a rare disease. But if so, was it worth while to deal with the question at all? It seems to me that the answer is in the affirmative. The man of science has to try to clarify every observation, however seldom it is made. But the reason why I discussed the topic at all was not the importance of syphilis of the pulmonary artery, but that of aortitis. This can and must never be overlooked, either in the present or in the future.

The ghost of aortitis haunts us constantly. Resistance against the modern antibiotics increases more quickly than we would have thought. In a most authoritative publication (O'Leary, 1950) we already read as follows: "It has been suggested by several antibiotists that within another five years penicillin will have vanished from the field." So the hope that syphilis may be completely eradicated in the not-far-distant future is fading. Under such circumstances we have to grasp with an eager hand every opportunity to deal with the subject of syphilitic arteritis, especially aortitis.

References.

Beermann, H., Nicholas, L., Buerk, M. S., and Ford, W. F. (1950), "Progress in Internal Medicine. Syphilis", *Archives of Internal Medicine*, Volume LXXXV, page 308.

Benecke, R. (1919), *"Ueber die Gefässerkrankung bei Syphilis und Nicotinvergiftung"*, *Münchner medizinische Wochenschrift*, Volume LXVI, page 1463.

Boyd, L. I., and Gawack, M. (1939), "Aneurism of the Pulmonary Artery; A Review of the Literature and Report of Two Cases", *American Heart Journal*, Volume XVIII, page 562.

Demography (1947), Commonwealth Bureau of Census and Statistics, Bulletin Number 65, Canberra.

Deterling, R. A., junior, and Clagett, Th. (1947), "Aneurysm of the Pulmonary Artery and Report of a Case", *American Heart Journal*, Volume XXXIV, page 471.

Groedel, F. M. (1939), "Aneurysm of the Pulmonary Artery", *Radiology*, Volume XXXIII, page 219.

Herxheimer, G. (1931), *"Syphilitische Veränderungen der Arteria pulmonalis"*, *Jadassohns Handbuch der Haut und Geschlechtskrankheiten*, Volume XVI, page 150.

Karsner, H. T. (1933), "Syphilitic Disease of the Pulmonary Artery", *Archives of Internal Medicine*, Volume LVII, page 366.

Martland, H. S. (1930), "Syphilis of the Aorta and Heart", *American Heart Journal*, Volume VI, page 1.

O'Leary, P. A. (1950), "The Changed Trends in the Treatment of Syphilis", *Collected Papers of the Mayo Clinic and the Mayo Foundation*, Volume XLI, page 304.

Rosahn, P. D. (1948), "Unknowns in the Biology of Syphilitic Infection", *The American Journal of Medicine*, Volume V, page 631.

Saphir, O., and Scott, R. W. (1930), "Observations on 107 Cases of Syphilis Aortitis, with Special Reference to the Aortic Valve Area, the Myocardium and Branches of the Aorta", *American Heart Journal*, Volume VI, page 51.

White, P. D. (1937), "Heart Disease", page 494.

Wile, U. I. (1948), "Some Obscure and Paradox Problems of Syphilis", *Archives of Dermatology and Syphilis*, Volume LVII, page 815.

TIGLOIDINE AS A SUBSTITUTE FOR ATROPINE IN THE TREATMENT OF PARKINSONISM.

By E. M. TRAUTNER,

Department of Physiology, University of Melbourne,

AND

C. H. NOACK,

Mont Park Mental Hospital, Melbourne.

WHEN the action of tropine and related alkaloids on the response of the muscle-stimulated isolated sartorius of the toad *Bufo marinus* was investigated (Trautner and McCallum, 1950), it was observed that some alkaloids gave a strong effect of "delayed recovery" (Shaw, 1947): repetitive stimulation at the rate of five to seven stimuli per second led to a progressive drop in action potential and to a considerable increase in the time of conduction of the successive responses, with complete abolition of response and contraction after 10 to 15 stimulations. This effect was temporary and the muscles recovered to their previous condition after a rest of a few seconds or more, depending on the intensity of the alkaloid action. This effect of delayed recovery was produced by all pharmacologically active alkaloids (atropine, hyoscyamine, apoatropine and hyoscine), but not by the pharmacologically inactive by-alkaloids, with one exception—namely, tigloidine, the tiglic ester of pseudo-tropine. Figure I shows electrical responses as obtained on repetitive stimulation, seven stimulations per second, with atropine, tigloidine and procaine, compared with those of an equimolecular mixture of tropine and tropic acid, of valeryl-tropine and of benzocaine.

On these observations it was considered whether tigloidine could replace atropine in the treatment of muscular diseases without causing the undesirable side-effects—dry throat, mydriasis and headaches. The toxicity of tigloidine was investigated on rats, rabbits and guinea-pigs; it was found that tigloidine in 100 times the lethal doses of atropine had no noticeable effect on the animals. Several patients suffering from Parkinsonism were treated with the alkaloid and showed good response One clinical history follows:

Report of Case.

H.B., a married woman, aged forty-seven years, had at the age of sixteen years an illness in which she "was very sleepy and saw double". Thereafter she had frequent oculogyric crises and suffered from increasing tremor in the hands and general muscular rigidity. The symptoms reached a maximum twelve years ago, when she was forced to enter hospital; she has been under hospital treatment ever since that time. Her condition is typical post-encephalitic Parkinsonism, rigidity being much more pronounced than tremor, and she has prolonged oculogyric crises. Untreated, she is practically bedridden, and is scarcely able to walk or to use her hands for dressing or eating, and her speech is almost unintelligible.

During these years she had treatment with several drugs suggested for Parkinsonism ("Parpanit", "Phenergan" *et cetera*), the most successful being atropine sulphate, five milligrammes taken two to three times daily. With this she was able to walk and to dress and feed herself, and her speech became clearer; the oculogyric crises were less frequent and severe, although they appear to have been

considerably less influenced than the other symptoms of the disease. However, this dose of atropine produced severe mydriasis, paralysis of accommodation, dryness of the mouth and a feeling of "fullness and tightness" in the head with constant headache, these last two being the most disagreeable symptoms.

On May 20, 1950, after one week without atropine medication, the administration of tigloidine hydrobromide was commenced in a dosage of 0·5 milligramme three times daily after meals. The dose was gradually increased, and on June 15, with a dosage of four milligrammes three times daily, lessening of rigidity, easier gait and more mobility of expression were observed. On July 5, at a dosage of 16 milligrammes of tigloidine given three times daily, there was further improvement, with less rigidity of arms, no "cog-wheel" rigidity and no tremor. The oculogyric crises were fewer and less severe; the pupils were slightly dilated, but her near vision was not appreciably affected. However, on July 7, with the same dosage, she complained that her vision was becoming worse for reading. The complaint was temporary, and the dosage of tigloidine was further increased. On July 26, when she had been taking 48 milligrammes three times daily for a week, her condition appeared to be better than at any time during the past few years with any treatment. Subjectively she felt no discomfort in the throat and—although her pupils were slightly dilated—no sensation of glare; she declared that she could read almost as well "as normally", and in particular she was completely free of the "stiffness and tightness behind the eyes and the forehead" and of the permanent headache caused by atropine. She said that the ocular crises were less severe and briefer, if not less frequent, than on any treatment previously given, but that she thought her legs were better with atropine. Objectively no difference in gait could be observed compared with that when she was under atropine treatment; the hands showed only little tremor and stiffness, but still reduced mobility, possibly due to years of comparative inactivity. The neck was freely movable, and she turned her head, apparently without effort, towards the person addressing her; apart from a drawing down and back of the right corner of the mouth, her facial muscles were free and reacted quickly with a smile, a frown or other expressions, and relaxed equally quickly. Her speech was perfectly clear and of normal speed; she seemed to be alert and to react quickly on changes in conversation. A temporary dosage of 64 milligrammes of tigloidine did not further improve the condition; it appears that the optimum beneficial effect of the drug in this case was reached with 40 to 48 milligrammes three times daily.

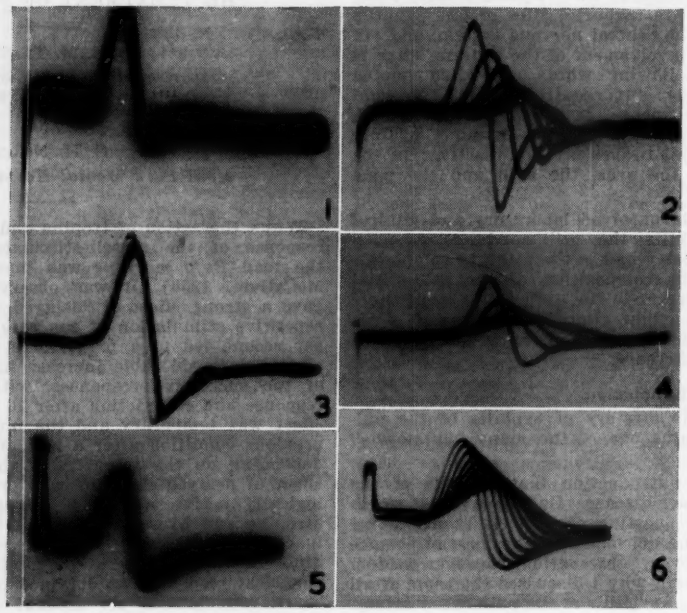

FIGURE I.

Superimposed action potentials of the muscle-stimulated isolated sartorius of the toad *Bufo marinus*. Oscilloscope records obtained by stimulation at the rate of five to seven stimuli per second with a constant voltage of two to three volts. Drug concentration, 1:1500 to 1:3000; time of drug action, twenty to thirty minutes. 1. Equimolecular mixture of tropine and tropic acid. 2. Atropine. 3. Valeryl-tropine. 4. Tigloidine. 5. Benzocaine. 6. Procaine.

Discussion.

Clinical Considerations.

Three other patients treated with tigloidine showed the same effect from the drug. The case recorded was chosen because the patient was alert and capable of reporting on herself; she has been treated with different medications and can compare the effects.

The beneficial effect of tigloidine was in all cases just objectively observable with a dosage equal to that at which atropine exercised its optimal effect. However, in the action on the isolated toad sartorius (Trautner and McCallum, 1950), the "delayed recovery" effect is of about the same order with equal concentrations of atropine and tigloidine. But it was found that attempts to elute the atropine from the muscles were not very successful; once it enters the tissue, the alkaloid is tenaciously retained and even a few hours of washing with frog Ringer solution will not completely remove it. Usually the muscle dies before it is completely detoxicated. Tigloidine seems to adhere less strongly to the tissue and to be more easily eluted. On the assumption that the intensity and duration of the drug action depend on maintaining a concentration in which the equilibrium between the all-over concentration of the drug in the tissue and that on the specific system, enzyme or other, is in favour of the latter, it was expected that higher amounts of tigloidine would be necessary to obtain equal effects in the living organism. The drug was given initially in small doses to ascertain that it did not cause undesirable by-effects not observable or not present in experimental animals, but later the dosage was rapidly increased.

The fact that increasing of the dosage from about 40 to over 60 milligrammes three times daily did not produce a further corresponding reduction of the symptoms, if any at all, suggests that in these cases of long standing the extent of possible improvement is limited. With atropine this limit could be approached only by the use of almost toxic doses, the unpleasant side-effects limiting the dosage; with tigloidine the dosage could be further increased, and it was possible to reach the optimum at which the tissue could respond to the establishment of more favourable conditions.

The effect of delayed recovery may be regarded as consisting in a quick but short-lived "fatigue", so that after a few stimulations the muscle responses are progressively weaker and finally disappear. It is considered that the action of atropine or tigloidine on the muscular system of patients suffering from Parkinsonism consists in lowering the threshold and partly abolishing the response of the muscle to those involuntary stimulations or other impulses which cause tremor as well as rigidity. At the present stage of the investigation no attempt is made to discuss the ætiology of the disease, and it is not intended to convey the impression that atropine and its homologues may exercise their effect by attacking the root of the disturbances. The observations made are equally compatible with the suggestion that the drugs merely effect a certain degree of relaxation of the muscle, and therefore allow it, to use Selye's terminology, to pass from a state

of exhaustion to a state of adaptation. The extent of this adaptation depends on the degree of relaxation which can be induced and on the power of adaptability still existing in the tissue.

Chemical Considerations.

The pharmacological effects of atropine and its nearer homologues—mydriasis, central and glandular effects and those on the smooth muscle—seem to depend on the esterification of the basic part of the molecule (tropine, scopine) with the aromatic tropic, atropic and mandelic

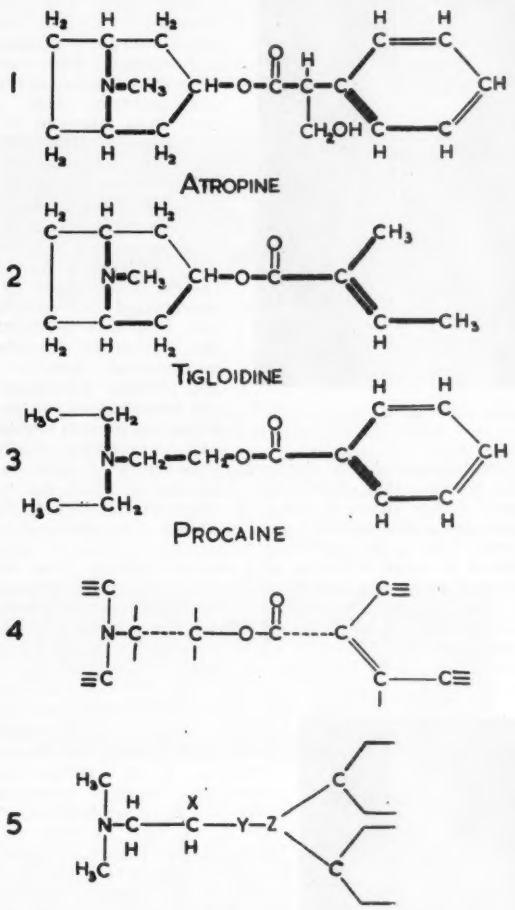

FIGURE II.

1, Atropine; 2, tigloidine; 3, procaine; 4, common groupings of the above compounds; 5, common groupings of antihistamine drugs with Parkinsonism-alleviating effect (Gair and Ducey, 1950). (X stands for hydrogen or methyl, Y and Z stand for C, O or N links.)

acids; they are lacking in all natural or synthetic products esterified with simple aliphatic acids, including tigloidine (formulas, Figure II). The latter, which is esterified with the unsaturated tiglic acid, shows the effect of delayed recovery on the isolated sartorius of the toad, while none of the by-alkaloids esterified with saturated acids shows this effect even in fairly strong concentrations (Trautner and McCallum, 1950), nor has any other physiological effect ever been recorded (*vide* Henri, 1949). Of the related heliotridine alkaloids, iso-heliotrine, which is esterified with saturated acids, showed no action, while lasiocarpine showed the effect. Since this alkaloid is esterified with the optical isomer of tiglic acid—namely, angelic acid—it was assumed that aromatic or aliphatic unsaturation in the acidic part of the molecule was necessary to produce the effect of delayed recovery in the muscle. Of compounds of related structure, procaine, pantocaine and others showed the effect; in the case of procaine the acid is *p*-amino-benzoic acid, while the basic part is the open-chain diethylamino-ethanol. Graubard and Peterson (1947) describe the beneficial effect of this drug on intravenous drip infusion of 0·1% solutions in spastic conditions, *paralysis agitans* and others. It would appear that the tertiary nitrogen atom does not need to be fixed in a ring structure. (Benzocaine, which lacks the nitrogen grouping in the esterifying alcohol, does not give the muscle effect of delayed recovery; its anæsthetic effect is determined by the *p*-amino grouping in the benzene ring and the esterlink only. Esterification with an amino-alcohol intensifies the anæsthetic effect, but opens also the way to other physiological effects beside the purely anæsthetic one.)

These observations are taken as indicating that in the action of atropine, tigloidine and procaine, the therapeutic effect on Parkinsonism and the muscle effect of delayed recovery are caused by the same fundamental grouping, possibly by the same mechanism of action. The common grouping consists of the following units (Figure II (4)): tertiary nitrogen—two or three methylene groups—alcoholic group esterified with either an aromatic or an unsaturated aliphatic acid, as marked in thick lines in the formulas of the active compounds. The advantage of atropine or tigloidine over procaine in the treatment of diseases like Parkinsonism lies in the fact that the two former can be given internally, being stable enough to reach the muscle before being metabolized, while procaine is rapidly hydrolysed in the body (Brodie, Ling and Poet, 1948), and would on slow intestinal absorption probably never reach a concentration sufficiently strong to have the desired therapeutic effect. Furthermore, intravenous drip infusion is not a practicable method for the treatment of "incurable" diseases.

The grouping $-CH_2-CH_2-N(CH_3)_2$ or $-N(C_2H_5)_2$ is an essential component of many synthetic antihistamine drugs. It is therefore not surprising that some of these also alleviate the symptoms of Parkinsonism; the effect can be expected if the connexion of the ethylamine over a linkage of one or two atoms with unsaturated systems causes sterically a certain degree of similarity of the resulting compounds. (However, this does not necessarily mean that there is a functional similarity between the two effects.) Figure II (5) presents the structural skeleton proposed by Gair and Ducey (1950) as characterizing those typical antihistamines which have a good or satisfactory effect on Parkinsonism. It is seen that the two ring-systems at the end of the molecule opposite to the ethylamine are not essential for the effect on Parkinsonism; one aliphatic double bond, as in tiglic acid, is sufficient.

Owing to the rarity of the naturally occurring tigloidine—it is found to 0·5% of the total alkaloids in some strains of the solanaceous shrub *Duboisia myoporoides*—it will not be possible to extend the clinical trials much further. However, the observations are considered as interesting enough to be recorded, because (*a*) they show the muscle effect of the drugs as being not connected with the other pharmacological effects—mydriatic *et cetera*, (*b*) they suggest a possibly useful formulation of the chemical groupings responsible for the therapeutic effect on Parkinsonism, and (*c*) they suggest a correlation between this therapeutic effect and the observations in a simple physiological test on the toad muscle.

Summary.

1. Tigloidine, the tiglic ester of pseudo-tropine, was tried as a substitute for atropine in four cases of Parkinsonism, after it had been found that its effect on the action potential and contraction of the muscle-stimulated isolated sartorius of the toad was identical with those of atropine.

2. The therapeutic effect of tigloidine on the symptoms of Parkinsonism was found to be identical with that of atropine, but tigloidine does not produce the undesirable

side-effect of the latter—namely, excessive mydriasis, dryness of the throat, gastric disturbances and severe headache.

3. The clinical and chemical significance of the observation is discussed, and the common chemical groupings of atropine, tigloidine and procaine are compared with those of the antihistamine drugs found to be beneficial in Parkinsonism.

Acknowledgement.

The authors wish to thank Messrs. T and H. Smith, Edinburgh, for a generous supply of tigloidine, which supplemented their own meagre stock.

References.

Brodie, B. B., Ling, P. A., and Poet, R. (1948), "The Fate of Procaine in Man Following its Intravenous Administration, and Method for the Estimation of Procaine and Diethylamine", *The Journal of Pharmacology and Experimental Therapeutics*, Volume XCIV, page 359.

Gair, D. S., and Ducey, J. (1950), "Chemical Structure of Substances Effective in the Treatment of Parkinsonism", *Archives of Internal Medicine*, Volume LXXXV, page 284.

Graubard, D. J., and Peterson, M. C. (1949), "The Therapeutic Uses of Intravenous Procaine", *Anesthesiology*, Volume X, page 175.

Henry, T. A. (1949), "The Plant Alkaloids".

MacCallum, M., McCallum, I. A. N., and Shaw, F. H. (1949), "The Action of Yohimbine on Excitation and Propagation in Nerve", *The Australian Journal of Experimental Biology and Medical Science*, Volume XXVII, page 115.

Selye, H. (1949), "Textbook of Endocrinology".

Trautner, E. M., and McCallum, I. A. N. (1950), "The Action of Tropine and Heliotridine Alkaloids on Excitation, Propagation and Recovery in Muscle", *The Australian Journal of Experimental Biology and Medical Science*, Volume XXVIII, page 343.

THE USE OF "PERSPEX" FOR SPLINTS.

By J. M. DAVIES, M.B., B.S.,

Assistant Medical Superintendent, Children's Hospital Orthopædic Section, Frankston, Victoria.

DURING the past year efforts have been made in the Children's Hospital Orthopædic Section, Frankston, to adapt a plastic material, "Perspex", as a medium from which splints of varying types can be made. Sheets of "Perspex" were generously donated by Imperial Chemical Industries, and two research chemists from this establishment were sent down to give technical advice and assistance with the manufacture of some of the early splints. The early experiments were prompted by a desire to find a material to take the place of plaster of Paris in cases in which lightness and lack of absorption were of considerable importance, and the first attempts were directed towards the manufacture of jackets, several of which were made and have been successful.

Basically the manufacture of any "Perspex" splint consists in the moulding of a sheet of "Perspex" around a previous cast of the limb or portion of the body to be splinted. This process presents a number of technical difficulties, and although we were helped by many suggestions from interested technicians, it has been found more satisfactory and more economical to entrust the actual moulding of the "Perspex" to a firm of plastic moulders.

Our initial efforts provoked quite a lot of mirth, as they were carried out in the hospital laundry, and consisted of the rapid transference of a sheet of heated "Perspex" from its improvised oven, either an autoclave or steam hot box, to a pre-warmed plaster "positive" and the rapid application of pressure through towels usually by as many as six willing helpers. Needless to say our first efforts were not very successful; but we then graduated to a pressure box designed by A. S. Fitzpatrick, D.Sc., consultant chemist, and consisting of a coffin-shaped box with a quick-release lid and a rubber diaphragm across the lower part of the lid. The plaster "positive" was placed on a sandy floor and the heated sheet of "Perspex" hurriedly placed on the positive, the lid clamped down, and a jet of compressed air introduced to the lid of the diaphragm which, theoretically at any rate, would mould the "Perspex" around the "positive". After shattering our very well constructed pressure box with too great a pressure of compressed air, we decided that sheet metal at least would be needed for further boxes.

FIGURE I.

Despite improvisation, several quite well fitting "Perspex" jackets were made, manual pressure only being used; these were made in an anterior and posterior half and were then trimmed to fit the patient. Illustrations for this appear below (Figures I to IV).

The main difficulties with "Perspex" jackets were those of correct fastening. As the jackets were bivalved, hinges had to be constructed at one side, and this was difficult as the curvature invariably necessitated hinging in two planes. Furthermore, the fastening of the jacket presented its own problems, and numerous methods were tried, probably the most satisfactory of these being the use of a long rubber lace engaging in small, flat "Perspex" cleats situated along the edges of the jacket. This provided some elasticity for breathing. The edges of these cleats had to be smoothed to prevent tearing of clothes, which is quite a factor with active children. One satisfactory jacket was made with parallel strips of duralium riveted to the posterior half and continued upwards to provide braces for a head support for a child with weak neck muscles. Difficulty was experienced with such jackets owing to their cracking; "Perspex" has to be treated gently, and will not stand abuse such as being dropped on a floor.

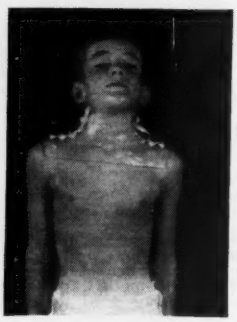

FIGURE II.

The next venture was the making of a bivalved "Perspex" collar for use by a patient suffering from cervical tuberculosis who was fit for ambulation. This collar, as may be seen in the photograph (Figure V), provided a good support both for the chin and for the occiput, the weight of the skull being carried on the shoulders, and having air ventilation holes it caused the skin no irritation. Here again small cleats were used with rubber lacing to fasten the collar.

Attempts were next directed towards the components of a type of "universal" splint—these components consisting of a head piece, a thoracic support, and forearm, thigh, leg and foot pieces, all of which could be mounted on movable carriers on to a basic tubular frame, telescopic at the joints, and with universal movements at shoulders, elbows and hips. Several of these frames have been in use now for six months or more, and whilst they have some disadvantages, do provide a comfortable means of immobilization in good position. The metal frame has been modified several times, and new ideas in this regard have been put forward by the splint shop staff at the Children's Hospital, Melbourne.

Our next venture was the manufacture of spicas for the nursing of small children suffering from poliomyelitis. These were found valuable, as the children could be nursed with their napkins on, provision being made for this during moulding. Furthermore, the sides of the "Perspex" could be made high enough and moulded tightly enough to prevent the external rotation of the upper parts of the thighs, which is so common a feature when hip muscles are affected. Numerous ventilation holes are of course necessary for these spicas. One particular case was interesting in that the child, as well as having a weak quadriceps, had a gross *talipes equino-varus* affecting the same foot; this was suitably splinted by an over-corrected Denis-Brown foot plate riveted onto the lower end of the spica.

Finally, our efforts were directed towards full-length "Perspex" beds for use in cases of spinal tuberculosis, and it is in this direction that "Perspex" has been most successful. So far four full-length "Perspex" beds have been made and used, and have proved most satisfactory, both in routine nursing and especially in post-operative care. The complete lack of absorption of any fluids—perspiration, urine, serum *et cetera*—has assisted greatly in cleanliness and lack of odour. When these children are turned onto an anterior turning case, a quick wash with soap and water renders the "Perspex" as new. The moulding of full-length beds presents great difficulties, so we entrust this task to a firm of plastic moulders, who have been most helpful in every way. Quite high pressures have to be used when a deep "draw" is needed, as, for example, around the head and shoulder pieces of the full-length beds. The latest of these beds has been made for a child on whom a bone graft to fuse a tuberculous sacro-iliac joint has been carried out, and the sides have been carried so high that lateral movement is impossible, and very little in the way of restraining straps is needed.

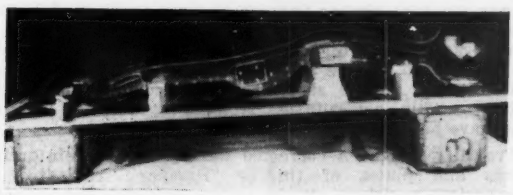

FIGURE III.

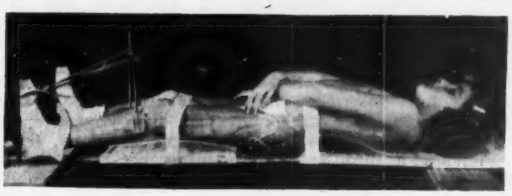

FIGURE IV.

Attention has been paid to the question of foot drop by the use of removable metal rods in sockets; from the top of these rods rubber strips are carried to sandals. These rods are recessed into holes in "Perspex" blocks or into the wooden frame on which the "Perspex" rests. It has been found advisable to make a wooden cradle for the support of the "Perspex" beds; handles on these cradles make lifting very easy, and the height of the cradle facilitates the giving of bedpans. The longest period over which one bed has been used is nine months, and it has proved popular not only with the child herself, but also with the nursing staff and with the medical officers in charge of the case, who were able to take X-ray pictures through the bed without any movement of the child's spine. As in all "Perspex" splints, numerous holes are drilled for ventilation, and these have proved effective.

Unfortunately the cost of these beds is high, being in the vicinity of £18; but with increasing use, this cost could be considerably lowered, and after the manifold advantages of such a bed have been weighed, the cost does not seem excessive.

Technique.

The manufacture of each type of splint presents its own problems, and an attempt will now be made to describe the commoner difficulties involved.

FIGURE V.

Jackets.

For cases of scoliosis it was found most suitable to make a plaster impression whilst the patient was suspended by the neck from a suspension frame supporting both chin and occiput, with the toes just touching the floor. For such a position to be used, each child had to be gradually accustomed to such suspension for an increasing period each day. This suspension, incidentally, proved of value in stretching the soft tissues which had accommodated themselves to the concavities of such scolioses. Care had also to be taken that the scapulæ were in correct position, and not rotated, as they would have been had both arms been allowed to hold the suspending pads. As will be appreciated, several assistants are necessary for the making of such an impression. When a plaster cast has set, it is cut vertically down the front, partially "sprung" and the child turned sideways; the jacket is eased off, then quickly bandaged into correct shape and allowed to dry thoroughly. The mould so formed is now filled with "plaster mud" into which a quantity of fibre, preferably "Sisal", has been thoroughly incorporated, and when this mud has dried the outer jacket is removed. To facilitate removal, it is advisable to smear the inside of the jacket liberally with "Vaseline" before pouring in the plaster mud. The resultant "positive" is now smoothed with further thin plaster mud and allowed to dry. Markings on this positive are now made with indelible pencil to show the margins of the required jacket, and it is ready for forwarding to the "Perspex" moulders for completion of the "Perspex" jacket. When it is fitted on to the child, any imperfections such as areas of increased pressure can be readily seen and dealt with by local heating and pressure with a cloth. Small brass hinges can be riveted along one side of the jacket, and the other side is fastened by the small cleats and rubber lacing already mentioned. In some cases it was found advisable to rivet small buckles on the upper margins of the jackets to which shoulder straps of webbing can be attached to prevent the downward slipping of the jacket.

Collar.

A complete impression of the patient's head, neck and shoulders was made, and for this purpose great assistance was obtained by the use of a dental material, "Zelex". This was plastered all over the child's head and shoulders, "backed" quickly with plaster bandages, the whole bivalved and removed, then fitted together again and bandaged to complete the mould. This was then filled with plaster mud as before, the mould was removed, and a perfect impression of the child's head, neck and shoulders resulted, onto which the necessary markings were inscribed, and the "Perspex" collar was moulded to these markings. "Zelex"

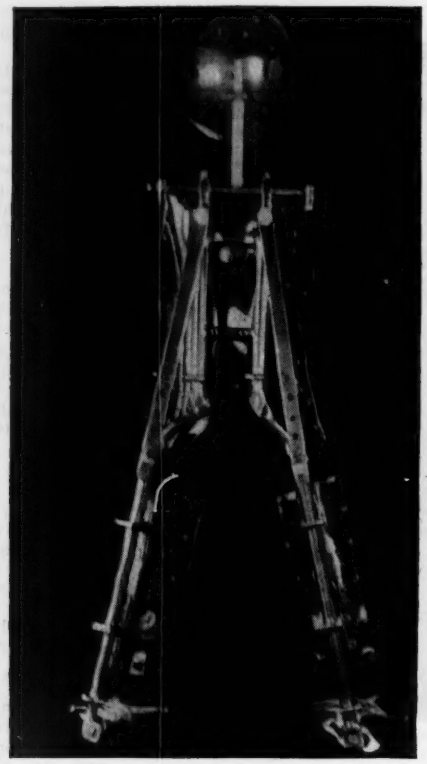

FIGURE VI.

has the advantage of being non-adherent to hair, but needs backing by some firm material for such a large mould. Such a collar, as can be seen in the photograph (Figure VI), provided good support for both the chin and the occiput, the weight of the skull being carried on the shoulders. Fastening again was carried out by small flat cleats and rubber lacing.

Beds.

A full-length impression in plaster of Paris was made with the child lying prone in the correct position—this being obtained by the use of pillows and appropriate padding—or, in cases in which hyperextension was needed, with the child lying prone on the reverse side of a Bradford frame. The use of a team to assist in the making of these full-length beds is essential to obtain adequate moulding, particularly around the head and shoulders, as the child has to be held firmly and accurately in position. The plaster mould so obtained is then lifted off, dried completely, lubricated with "Vaseline", and then filled with plaster mud impregnated with "Sisal". This reinforcement was found to be essential, especially if there is any hyperextension, as the pressures needed to mould the "Perspex" caused breaking of non-reinforced plaster "positives". The use of wooden cradles adds greatly to the ease in nursing, and, of course, facilitates the taking of X-ray pictures, as the plates can be held under the "Perspex" bed. These cradles are of necessity made after the "Perspex" bed has been completed, and are lined with thick felt where the wooden supports touch the "Perspex".

Universal Splint.

Components for the universal type of splint can be made from a "positive" made in the same way as has been described for the making of a bed, the extent of each component being marked on the "positive" with indelible pencil for the guidance of the moulding firm.

Summary.

The use of a plastic material, "Perspex", for the manufacture of a variety of splints is discussed. It has disadvantages, including high initial cost, fragility, additional labour (in that plaster "positives" have to be made), and unsuitability for moulding directly onto the skin; but it has advantages in that it is light, impervious to fluids, transparent to X rays and to actinic rays, easily cleaned, non-irritating to the skin, and most comfortable to the patient. This last point is stressed by all the patients who have been nursed in this type of splint.

Fragility has been corrected by the use of reinforcing bands and plates of thicker "Perspex", cemented in appropriate positions on the splint, and one bed so reinforced has shown no signs of cracking in the nine months over which it has been used.

Acknowledgements.

I am greatly indebted to Dr. Douglas Galbraith, the superintendent of the hospital, for assistance and encouragement in the manufacture of these splints. I am indebted also to Dr. John Colquhoun and Dr. Eric Price for permission to try "Perspex" for the splinting of their patients, and for advice in the use of these splints. I should also like to acknowledge the assistance given by Imperial Chemical Industries of Australia and New Zealand, Limited, who not only supplied free of charge several sheets of "Perspex" for our initial experiments, but also made available two of their experts to render technical advice. Dr. A. S. Fitzpatrick, consultant chemist, was also most interested in this work, and spent many hours preparing designs for the pressure box. A local firm of plasterers, Universal Plastering Company, led by Mr. F. Wagg, a fibrous plaster manufacturer, gave valuable advice, and have helped in the making of our moulds, pointing out the desirability of using reinforcing material such as "Sisal". The engineering firm of A. E. Atherton and Sons helped with the metal components of the frame for the universal type of splint. Finally, the firm of plastic moulders, Godfrey and Lynch, have been most enthusiastic throughout our experiments, and go to endless trouble both in the making and in the fitting of each individual splint.

INTRACRANIAL ABSCESS FOLLOWING FRONTAL SINUS INFECTION.

By R. S. HOOPER,

Department of Neurology and Neurosurgery, Royal Melbourne Hospital, Melbourne.

THE difficulty experienced in the diagnosis of intracranial complications extending from a recognized frontal sinus infection is well known; but almost as frequently one encounters an intracranial complication when the primary frontal sinus infection has not been recognized. In consequence, this difficult problem is likely to be encountered by physicians almost as frequently as by oto-rhino-laryngologists.

The main weight of the problem must fall on the physician, upon whom the responsibility for early diagnosis rests. This is a problem of considerable difficulty, and frequently the final and positive diagnosis is the prerogative of the neurosurgeon. Occasionally this is left to the morbid anatomist.

This paper results from a survey of twelve cases in which the frontal sinusitis was complicated by some intracranial extension, and an attempt will be made to illustrate the difficulties in diagnosis, and to indicate methods by which these may be overcome.

The first case in this series illustrates in rather extreme form the difficulty in obtaining a diagnosis before some cerebral catastrophe occurs.

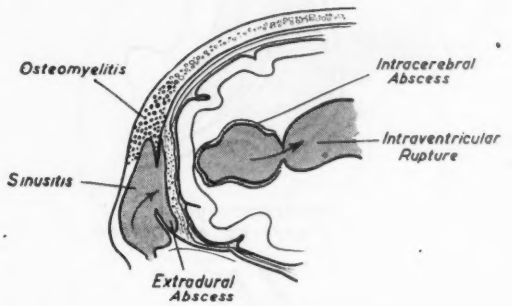

FIGURE I.
Diagram illustrating the extensive spread of infection in Case I.

CASE I.—The patient, aged twenty-three years, walked into a military hospital one evening, having been sent in from an outlying station where he had complained of headache and irritability. He was examined by the resident medical officer, and X-ray examination and a lumbar puncture were ordered for the morning. At 3 a.m. he suddenly became comatose. Opisthotonic spasms with stertorous breathing, cyanosis and hyperpyrexia followed, and death occurred in less than half an hour. It was not difficult to diagnose an intraventricular rupture of a cerebral abscess. This was confirmed at autopsy, at which a complete series of complications was seen (Figure I).

Purulent empyema of the frontal sinus had been followed by osteomyelitis and erosion of the posterior wall of the sinus, so that an extradural abscess formed. A considerable amount of inflammatory thickening and exudate was present over both surfaces of the dura, the inner surface being adherent to the pia arachnoid, and around this area leptomeningitis was apparent. In the substance of the frontal lobe a partially collapsed cerebral abscess had discharged its contents into the lateral ventricle, which contained purulent fluid.

A review of the history of this case provided little indication of the condition until all the clinical features—headache, alternate irritability and apathy, and transient swelling of the eyelid—could be correlated and their importance realized in view of the pathological possibilities.

The pathological possibilities should give rise to little difficulty. The extension of infection from the frontal sinus tends to follow a pathological sequence in which each layer is traversed in its turn by the infection. Thus, every case may follow the sequence illustrated in Figure II: (i) purulent inflammation of the muco-periosteum, (ii) osteomyelitis, (iii) *pachymeningitis externa*, (iv) *pachymeningitis interna*, (v) leptomeningitis, (vi) cerebritis or encephalitis (uncommon except in the early stage of abscess formation), (vii) cerebral abscess, (viii) intraventricular rupture.

Although certain planes may appear unaffected by the passage of the infection across them, it is important to be able to visualize the pathological possibilities in any particular case.

It is important to have some knowledge of the relative frequency of these conditions. Although the present series is small, it is reasonably representative, and gives an indication of the incidence of the various complications. These are shown in Table I.

Rearranging these results and setting out the complications in order of frequency, we find in Table II that osteomyelitis is the commonest complication, then follow intracerebral abscess and next meningitis. It will be seen from these tables that there is an obvious relation between osteomyelitis and the development of an intracranial abscess. Only one patient who developed osteomyelitis failed to develop either a subdural or an intracerebral abscess. Even in a small and possibly selected series this is a significant finding. For this reason intracranial suppuration must be suspected, and if necessary, excluded by ventriculography when frank osteomyelitis is present.

Secondly, it will be seen that there is a close relation between thrombophlebitis and subdural abscess, and, as will be seen later, with convulsive attacks.

Comparison with a similar series of intracranial complications following otitic infections indicates that subdural abscess is relatively more common in association with frontal sinus disease than in primarily otitic infections. On the other hand, meningitis as an isolated complication appears much less frequently than in otitic infections, provided one does not include the infections following fractures through the frontal sinus; this type of meningeal infection is more common than that following fractures involving the middle ear.

An analysis of the clinical features provides some interesting data.

Positive evidence of frontal sinus suppuration before the discovery of the intracerebral abscess was found in only two cases. These two case histories are of interest.

TABLE I.

Complication.	Case Number.											
	I.	II.	III.	IV.	V.	VI.	VII.	VIII.	IX.	X.	XI.	XII.
Sinus infection	+	+	+	+	+	+	+	+	+	+	+	+
Osteomyelitis	+		+		+	+	+	+	+		+	
Extradural abscess or superficial abscess	+					+		+	+			
Pachymeningitis externa	+		+					+			+	
Pachymeningitis interna or subdural abscess	+			+	+	+						
Thrombophlebitis	0			+	+	?						
Meningitis	+			+	+	+	±			+		
Intracerebral abscess	+	+	+				+	+			+	+

CASE II.—J.D., aged twenty-nine years, in spite of confirmed frontal sinus suppuration, orbital œdema, papilloedema, drowsiness and mild pyramidal signs, was not referred for a surgical opinion until he had lapsed into a stuporose state. At this stage the abscess was aspirated twice, and then a few weeks later the whole cavity was excised.

This case is of interest because it occurred before the days of penicillin, thus illustrating the fact that the general principles of treatment can be applied even without the help of the recent chemotherapeutic agents.

CASE IV.—Another patient was receiving treatment for chronic otorrhœa when she became drowsy and stuporose. Several convulsive seizures occurred. At operation no otitic abscess was found, but a large frontal subdural collection closed, and through burr holes placed behind the hair line, a penicillin tube was placed in the subdural space and intraventricular and subdural penicillin therapy was commenced. Subsequent recovery was rapid and uneventful, though he was left with a cranial defect which later required a plastic operation.

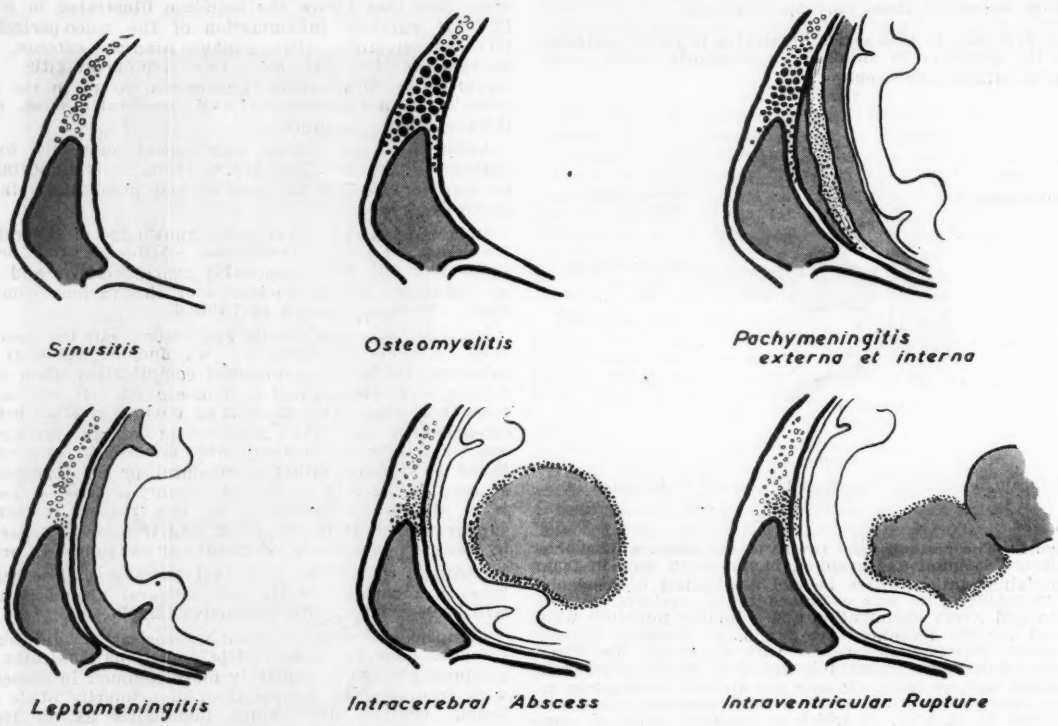

FIGURE II.
Diagram illustrating the range of infective complications which may follow frontal sinusitis.

In the second case the local and intracerebral infections appeared manifest at the same time. The intracranial collection was revealed after a radical operation upon the frontal sinuses. Although the extension of this operation at that time was a life-saving procedure, it was not adequate to control the infection completely, and the resulting deformity was severe.

TABLE II.

Complication.	Number of Cases.
Osteomyelitis	8
Intracerebral abscess	7
Meningitis	3
Subdural abscess	2
Thrombophlebitis	6

CASE VI.—D.F., aged seventeen years, after a five-day history of orbital swelling, irritability and convulsions, was subjected to a radical frontal sinus operation. Osteomyelitis and extradural and subdural collections of pus were encountered, and the incisions and bone removal were extended. Progress was not entirely satisfactory and he was admitted to hospital for further treatment. He was then in a state of semicoma, with absent reflexes. The frontal wound was drained, and later, when the frontal sinuses were opened, these were found to contain pus.

Apart from these definite cases, five other patients complained of colds, influenza or sinus troubles in the three weeks prior to the cerebral manifestations.

In three cases there was no history relative to the affected sinus, as in the following:

CASE VII.—J.C., aged eleven years, after four days of progressive drowsiness and stupor, was found to have cerebro-spinal fluid under a high pressure, and on examination it contained 40 polymorphonuclear leucocytes per cubic millimetre. Burr holes were made to exclude the presence of an abscess, and a large frontal abscess was encountered. The pus was aspirated, and 40,000 units of penicillin and two millilitres of thorotrast were instilled. Subsequent radiographs (Figure III(*a*)) showed a large abscess lying behind a frontal sinus whose shadow was abnormal. When a more careful history was taken, transient swelling of the eyelid on the affected side was found to have preceded the onset of drowsiness. Intermittent aspiration and penicillin instillation were continued for fourteen days, when the abscess outline had been reduced to a narrow crenated shadow (Figure III(*b*)).

Œdema of the eyelid (ascertained at a later stage in this case) is an important sign in a condition in which positive signs may be scarce and elusive.

Changes in mental state were often slight in the earlier stages, but irritability, mild personality changes and forgetfulness were present in almost all cases. Unfor-

tunately, these are symptoms which can be elicited only if relatives are sufficiently observant or the patient is sufficiently cooperative.

Convulsive episodes are a more dramatic manifestation of intracranial complication. In this series all three subdural abscesses were manifest by epileptic seizures, while this symptom was absent in all the intracerebral abscesses. The presence of cortical thrombophlebitis was confirmed in two of the patients with subdural abscesses, and it is believed that this lesion is probably the commonest cause of epilepsy among the pathological conditions following frontal sinus infection.

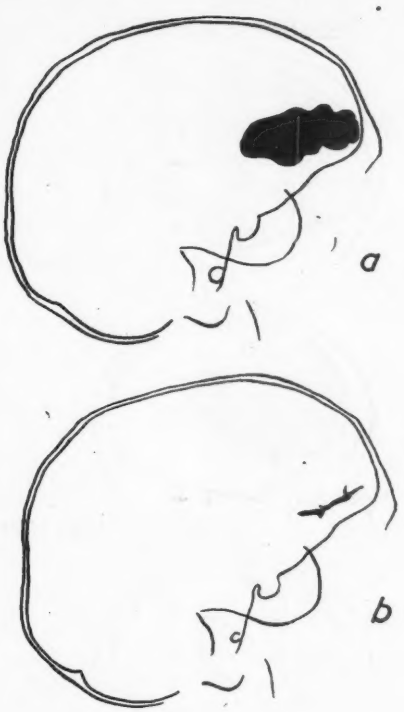

FIGURE III.

Tracings of radiographs in Case VII: (*a*) the large frontal abscess outlined by the radio-opaque thorotrast; (*b*) the narrow crenated shadow of the collapsed abscess cavity in the final stage of treatment.

CASE IV.—R.A., aged eight years, had both ear and sinus infections which did not subside satisfactorily with simple drainage of the subdural abscess; for this reason an osteoplastic flap was elevated. Masses of exudate and pus were evacuated, and beneath this accumulation thrombophlebitis of the cortical vessels overlying Broca's area was seen. This accounted for the localized convulsive phenomena and the aphasia. Drain tubes for penicillin instillation were placed at vantage points, and generous decompression was allowed. Subsequent recovery was straightforward.

Drowsiness, stupor and coma indicate a rise of intracranial pressure beyond the limits of intracranial compensation, and are in themselves urgent warnings for a rapid clarification of the position. In some cases this was the only indication of an intracranial pathological lesion. In such cases (for example, in Case VII) the diagnosis may rest between cerebral abscess, a rapidly growing tumour and tuberculous meningitis. Diagnostic procedures must be carried out rapidly and relentlessly till a positive diagnosis is made.

Other signs of increased intracranial pressure are inconstant. Papilloedema occurred in only five cases; dilatation of the ipsilateral pupil was seen in the same number. Third and sixth nerve pareses were present in the same proportion.

Some degree of fever was obvious in six cases, but in only six were there signs indicative of a meningeal reaction. These were slight in two cases and severe in two cases; in two other cases lumbar puncture was contraindicated in the early stage owing to evidence of high intracranial pressure.

With the introduction of the electroencephalograph it was hoped that this instrument would prove an important aid in the early diagnosis and localization of cerebral

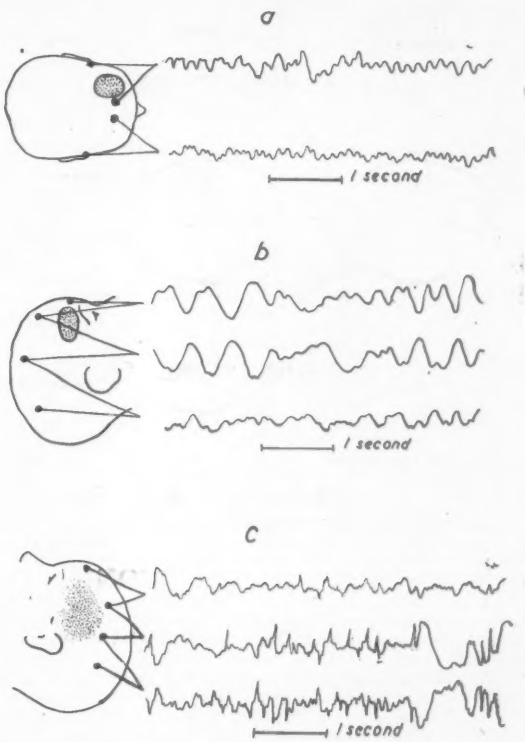

FIGURE IV.

Electroencephalographic records in three cases: (*a*) Case XI: six waves per second confined to the affected frontal lobe; (*b*) Case XII: high voltage two to three waves per second, which appear out of phase; (*c*) Case IV: random and rapid spikes associated with thrombophlebitis and subdural abscess.

abscesses. In the later abscesses of the series this instrument did prove a valuable help, revealing a focus of abnormal activity manifest by "out of phase" high voltage slow waves (two or three per second) in Case XII (Figure IV(*b*)), or a characteristic rhythm (four to seven waves per second) over a circumscribed area (Figure IV(*a*)). In those cases associated with thrombophlebitis (Case IV) bursts of epileptic activity are seen as in Figure IV(*c*).

Although it may be said that it is not possible to exclude a cerebral abscess by electroencephalography, this procedure will frequently localize the affected area. The following case illustrates the localization in this manner after a failure by ventriculography and angiography.

CASE XII.—A.W., aged nine years, complained of right frontal headache and vomiting, of five days' duration. There were no localizing signs, and only a mild degree of papilloedema and some neck stiffness were present. Cerebrospinal fluid was obtained at a pressure of 270 millimetres, and examination revealed 80 lymphocytes per cubic millimetre and 80 milligrammes of protein per 100 millilitres. The chloride content was 760 milligrammes per 100 milli-

litres. A ventriculogram was prepared; the left ventricle was found to be displaced to the left, but the right ventricle could not be filled. Subsequent exploratory aspiration could not localize the abscess. An angiogram was prepared, and this again revealed a displacement of the mid-line vessels to the left, but no other localizing feature. An electroencephalogram was then prepared, and this revealed a circumscribed area of abnormality in the right frontal lobe, from which high-voltage slow waves were obtained, which exhibited a difference in phase in anterior and posterior frontal leads (Figure IV(*b*)). The brain was again aspirated in this region and a large abscess found immediately behind the right frontal sinus. This structure, although poorly developed, radiographically showed mucosal changes.

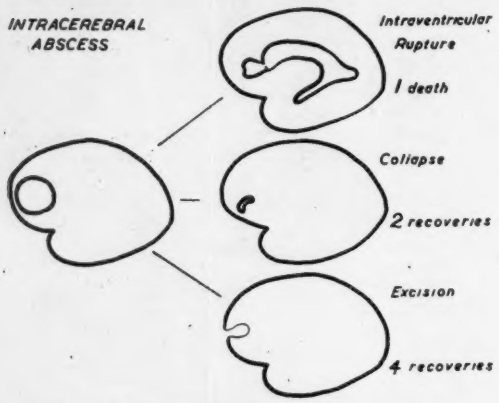

FIGURE V.
Diagram representing the results obtained in seven cases of intracerebral abscesses.

After repeated aspiration and penicillin instillation the abscess cavity contracted down to a small shrivelled scar, and no further operative measures have been carried out in this area.

An analysis of the clinical manifestations produced by these complications is difficult. But the patients do fall into three main clinical groups, as follows: (i) Those with apparent signs of local sinus infection, who gradually develop indications of an expanding intracranial lesion. Four patients presented in this manner. (ii) Those in whom a mild upper respiratory infection was followed rapidly by acute cerebral involvement, manifest by convulsions or the rapid development of coma. The catastrophic onset was seen in three cases. (iii) Those who slowly developed signs and symptoms of an intracranial space-occupying lesion without evidence of its origin. This problem was presented by three patients.

On the basis of this experience, is it possible to outline the general principles in the management of such cases? As diagnosis is the essential requirement for management, what are the steps to be taken to finalize diagnosis? In order of application they may be set down thus: (i) the noting of suggestive clinical features; (ii) the noting of suggestive electroencephalographic findings; (iii) exploratory needling; (iv) ventriculography; (v) arteriography.

Diagnosis.

The definite diagnosis of a frontal abscess cannot be made until pus has been demonstrated. In one case this was not done until the post-mortem examination, while in another pus was found during a radical frontal sinus operation. In the remaining eight cases pus was obtained after an exploratory trephine and aspiration. In only one of these cases was the condition sufficiently obvious for a confident pre-operative diagnosis to be made. In the remainder the main indication for exploratory aspiration was the steady deterioration of consciousness due to raised intracranial pressure probably of inflammatory origin. Localization was assisted by ventriculography in three cases, and by electroencephalography in three cases.

Radiographs of the skull may show a loss of translucency either of the frontal sinus or of the surrounding bone if osteomyelitis is present. These signs are helpful if observed, but their absence may be misleading. In the first case described, the frontal sinus shadow was normal. The density of the empyema of the sinus was offset by the erosion of the posterior wall, while in others the radiographic demonstration of bone rarefaction lags behind the inflammatory process.

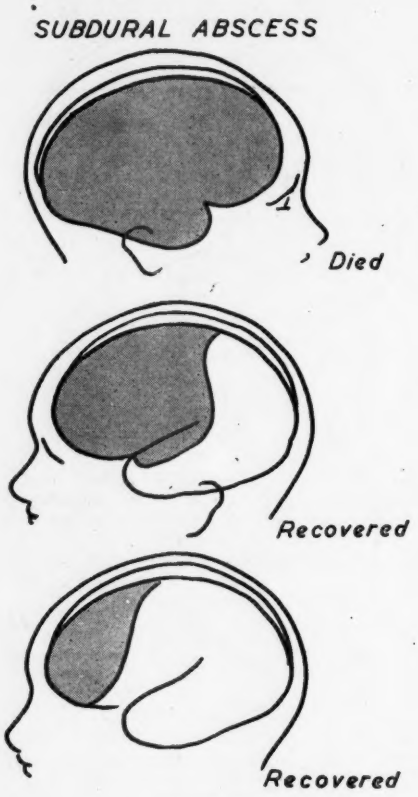

FIGURE VI.
Diagram representing the results obtained in three cases of subdural abscesses. The shaded portions represent the extent of the purulent collections.

The diagnosis of the intracranial lesion as a complication naturally depends upon the recognition of a frontal sinus infection. As the foregoing notes illustrate, this is not always a simple matter. A suggestive history is not easy to obtain from a drowsy, uninterested patient; local signs may be fleeting and the radiographic appearance misleading.

The diagnosis of a frontal lobe disturbance can rarely be made on symptoms and signs alone. Lumbar puncture, although it may serve to reinforce the suspicion of an intracranial complication, gives little help in its differentiation and localization. As an early diagnosis is an essential requirement for successful management, it must be realized that exploration must be carried out without delay in order to establish the presence or absence of the most important complication, intracranial abscess.

Considerable assistance in diminishing the range of exploratory aspiration may be obtained by electroencephalography, ventriculography or angiography.

Management.

Since the introduction of penicillin the management of osteomyelitis and meningitis presents little difficulty, and these will not be discussed separately. Of the remaining suppurative collections, the management after localization of pus has become a relatively simple procedure, though it differs for intracerebral and subdural abscesses. As these methods are now widely accepted, they will be described in summary fashion as an introduction to the results obtained.

When the intracerebral abscess is first localized by the exploring needle, pus is gently aspirated. This material is examined by culture and the organism tested for its sensitivity to antibiotics. Penicillin solution (10,000 units per millilitre) is then introduced into the cavity, and finally one or two millilitres of thorotrast are instilled. Radiographs of the skull are obtained, and an accurate estimate of the size and relation of the abscess is made. Aspiration of the cavity and instillation of penicillin are then repeated at intervals of one to five days until the subsequent radiographs show that the cavity, now delineated by the thorotrast taken up into the walls, has shrunk; at the same time the walling-off process continues. In some cases the radiographs show that the abscess cavity becomes a crenated, shrivelled scar (Figure III), and in these no further treatment is necessary. On the other hand, the abscess may not collapse entirely, and in these cases it seems wise to excise the abscess cavity together with the infective tissues along the pathway of the infection. An osteoplastic flap is elevated and the abscess is dissected out like a localized cerebral neoplasm. At the same time, it is easy to remove the posterior wall of the frontal sinus, strip away the mucous membrane and thus remove the source of infection. The advantage of this procedure is that no visible scar or deformity of the frontal region remains.

The management of subdural collections would be a much simpler matter were it not for the tendency for the pus in this situation to become loculated. When the pus is obtained through the exploratory burr hole, it is examined by culture and the penicillin sensitivity of the organism is estimated. If the collection appears large, further bone openings are made and fine tubes introduced for drainage and instillation of penicillin solution. In some cases the infection clears up rapidly, while in others progress appears unsatisfactory and ventriculography must be carried out to determine whether a further loculus remains without drainage. In some cases the presence of thick exudate precludes drainage, and in these an osteoplastic flap may be required for the removal of exudate and the placing of penicillin tubes at vantage points within the cavity.

In only one case was a plastic procedure necessary to remedy a cosmetic defect.

Results.

The results of modern methods must be considered satisfactory if an early diagnosis can be obtained. An analysis of the results shows that the bone infection and meningitis clear up on intensive treatment with antibiotics. It may be observed here that when osteomyelitis is present, penicillin therapy must be continued for eight weeks. If sequestra form before the infection is controlled, they will require removal; they are not common after the infection has been controlled.

Seven intracerebral abscesses occurred in this series (Figure V). Death occurred in only one case; this patient was not examined until intraventricular rupture had taken place. All the remaining patients recovered without organic defect, the abscess being excised in four cases. In only one case has post-operative epilepsy occurred. Of the three patients who had subdural collections (Figure VI), one patient, who had been in *status epilepticus* for forty-eight hours, was almost moribund when the cavity was evacuated, and died during an epileptic seizure some hours after evacuation of the pus. The remaining two patients recovered, one with drainage alone, the other after an osteoplastic flap had been elevated and exudate removed. This last patient had a recurrence of the sinus infection with meningitis, which subsided when intrathecal penicillin therapy was instituted. A radical sinus operation was then carried out.

The results of treatment are shown diagrammatically in Figures V and VI.

Conclusion.

The outstanding conclusion to be drawn from this series is that the treatment of intracranial complications of frontal sinus disease is easy, but the diagnosis is difficult. Symptoms and signs referable to frontal sinus infection may be slight or absent. Transitory local signs may precede the intracranial extension for some days, and may be forgotten with the development of more urgent and even catastrophic manifestations of cerebral involvement.

Because modern methods of treating these complications are so satisfactory, it is essential that diagnosis must be pursued relentlessly to a conclusion.

Summary.

The clinical features of 12 cases of intracranial complications of frontal sinus infection are discussed.

The difficulties in early diagnosis are illustrated in all cases of the series.

The principles of management are outlined, and results obtained are surveyed.

OLIGOPHRENIA PHENYLPYRUVICA, OR FØLLING'S DISEASE.

By S. J. CANTOR, D.P.M.,
Melbourne.

IN 1934 Professor Asbjorn Følling, of the physiological department of the Veterinary College and Genetics Institute of the University of Oslo, first described the syndrome or disease which now bears his name and which is also called phenylpyruvic oligophrenia. In this disease mental deficiency of slight or severe extent is associated with the excretion of phenylpyruvic acid in the urine and with other characteristics. He gave an account of ten patients who suffered from the disease (Følling, 1934).

The ailment, which is hereditary in origin and which is determined by a single recessive gene, results from the faulty metabolism of the product of the digestion of protein, the amino acid phenylalanine. The disease in its hereditary origin is not sex-linked.

In a subsequent paper the writer will give a more detailed account of the condition as well as a description of three cases which have been noted at the Children's Cottages for mentally defective patients at Kew. This paper has been written to draw attention to this rare disease; to suggest a possible nationwide survey to ascertain the incidence in Australia; to take such steps as may be possible to reduce the incidence; and to stimulate interest in the associated biochemical problems, which are important problems in protein metabolism. The incidence of the disorder, it may be added, is 1 in 15,000.

The Test for Phenylpyruvic Acid.

Phenylpyruvic acid is easily detected by the addition of *Liquor Ferri Perchloridi* to the urine. A teaspoonful of the latter is required, and several drops of the ferric perchloride solution are added. The test may be carried out in a test tube as a ring test, the perchloride solution being put in first. A dark green colour appears, which fades away in a few seconds or in a minute or so. If the urine is alkaline it may be made slightly acid with a few drops of dilute sulphuric acid. Urine may be preserved

if necessary with a few drops of toluene; this does not interfere with the test.

The Nature and Problems of the Disease.

Følling, in his first account of the condition, called it phenylpyruvic imbecility, as the investigations were carried out in hospitals for imbeciles. Jervis, in 1937, suggested the present name.

Later (Følling, Mohr and Rudd, 1945) a survey was made in Norway to determine the incidence of the disease, and physicians were asked to apply the ferric chloride test to the urine of all mentally defective patients in their districts. All patients who gave positive results were subject to expert control. Case histories and pedigrees were also obtained. A total of 1520 mentally defective patients were examined; of these, 23 were found to suffer from phenylpyruvic oligophrenia.

The scheme of inquiry (the notes have been made from the article by Følling and his associates) contained columns for the name, date of birth, place of birth, address, reaction (*plus* or *minus*) and special remarks. In addition it contained columns for further information on those subjects whose urine gave a positive reaction: the approximate degree of mental disturbance, somatic complications, family information, complications and treatment. The ultimate incidence found by the extended survey was 34 cases among 2400 mental defectives, a percentage of 1·4. Pedigree data made it possible to trace eventual common descent of fraternities with affected individuals.

The problem of the disease, apart from the hereditary factors, lies in the incomplete knowledge of protein metabolism. Phenylalanine, one of the amino acids produced as the result of the digestion of protein, can be changed in the body to hydroxyphenylpyruvic acid, which in turn can be transformed into tyrosine; but tyrosine cannot be changed to phenylalanine. This latter can be changed into phenyllactic acid, which, as well as phenylalanine, appears in excess in the blood in the disease. Phenylpyruvic acid is not found in the blood; it is produced in the kidneys from phenylalanine; it appears in consequence in the urine. In phenylpyruvic oligophrenia phenylalanine or one of its derivatives acts as a poison to the central nervous system.

In the Norwegian survey it was found that a high degree of consanguinity, such as the marriage of first cousins—if they carried the causative recessive gene—resulted in a higher familial incidence of the malady. It is to be noted that through the phenylalanine-derived toxin the gene influences the nervous system with resulting mental deficiency, the posture (which is one of rigid flexion), the muscles (which are hypertonic), the skin (which is fair in colour), the hair (which is usually flaxen), the eyes (in which the iris is blue), and the general metabolism as evidenced clinically by the appearance of phenylpyruvic acid in the urine. The parents of patients are almost always normal mentally; generally they are Nordic blonds.

Signs and Symptoms.

The signs and symptoms are, as has already been stated, mental deficiency, neurological signs and the excretion of phenylpyruvic acid in the urine. Most patients have blue eyes, pale skin and fair hair. The stroma of the iris is usually loose in texture. There are no stigmata of degeneration.

The degree of mental deficiency varies. Some patients are hopeless idiots, unable to do anything for themselves. Others are imbeciles, able perhaps to do some work under supervision. Others again can be described as retarded or backward children. In the Norwegian survey some patients were found to be able to earn a little money by their handiwork, or even to pass the final examination at the primary class. Some of these patients at a superficial examination would hardly be suspected of being feeble-minded.

It was also found that the daily quantity of phenylpyruvic acid excreted in the urine when an ordinary diet was taken varied from patient to patient and that there was some degree of correlation between the amount excreted and the degree of mental deficiency. It was noted in addition that a trained worker could pick out the patients at a glance among a group of mental defectives.

Neurological signs may be absent. Tremor, muscular rigidity, active deep reflexes and athetosis may sometimes be noted. In the cases at Kew neurological signs were unimportant. No pigmentation of the skin has occurred in the one patient who, as an imbecile, is an outside worker.

Følling and his co-workers as well as other writers have pointed out that the excretion of phenylpyruvic acid is increased when patients are given *l*-phenylalanine *per os* and when they are put on a diet rich in protein. No other amino acid has been found to alter the excretion rate of phenylpyruvic acid. In normal persons up to 15 grammes *per os* of *l*-phenylalanine produce only a trace of phenylpyruvic acid in the urine; but *d*-phenylalanine given to normal persons causes large quantities of phenylpyruvic acid to appear in the urine. This transformation of *d*-phenylalanine, according to Følling, is believed to be due to the enzyme *d*-aminoacid desaminase found by Krebs in 1933 in the liver and kidneys of different animals, the coenzyme of which was isolated by Warburg and Christian in 1938.

In 1941 Closs and Braaten injected absolutely *d*-free *l*-phenylalanine into nephrectomized rats; an increase of *d*-phenylalanine occurred in the blood. In more recent years valuable work on the associated problems of amino acids in the blood has been carried out with labelled radioactive carbon in the amino acids and by means of the technique of paper chromatography.

Discussion.

Phenylpyruvic oligophrenia is due to a single gene; the result is faulty metabolism of the amino acid phenylalanine. The diagnosis is made by finding mental deficiency, the body characteristics, and the presence of phenylpyruvic acid in the urine.

Følling has noted that in two cases a normal parent of two affected children married a second time; in the second marriage these parents had seven and five children respectively, all of whom were normal. It is to be presumed that in the first marriages both male and female had the recessive gene; in the second marriages only the males had the responsible genes.

Summary.

Three cases of phenylpyruvic oligophrenia have been found to exist in Victoria.

The work of Følling and others has been reviewed. It is suggested that, as was done in Norway, a survey should be made.

Acknowledgements.

The advice and cooperation of Professor V. M. Trikojus and of Associate Professor W. A. Rawlinson, of the School of Biochemistry, University of Melbourne, as well as of Dr. Robert Southby, immediate past president of the Victorian Branch of the British Medical Association, is acknowledged. The Clinical Research Laboratories of the Royal Melbourne Hospital, under Dr. Ian Wood, have also helped.

Permission to publish this article has been given by Dr. J. Catarinich, Director of Mental Hygiene.

References.

Følling, A. (1934), "Oligophrenia Phenylpyruvica", *Hoppe Seyler's Zeitschrift für physiologische Chemie*, Volume CCXXVII, page 169.

———, Mohr, O. L., and Rudd, L. (1945), "Oligophrenia Phenylpyruvica".

Warburg, O., and Christian, W. (1938), *"Co-ferment der d-Aminosäure-deaminase"*, *Biochemische Zeitschrift*, Volume CXCV, page 261.

SOME PSYCHO-PHYSICAL ASPECTS OF BACKACHE.

By E. HASLETT FRAZER,
Sydney.

THIS is a brief, and I hope somewhat practical, account of a method of approach to the problem of backache. It has been evolved after twenty-five years, spent almost exclusively in the treatment of the psychoneuroses and arthritis. That these two apparently unrelated diseases are very closely allied has always been my conviction.

Man is a tripartite animal, not always, unfortunately, of a high degree of emotional, ethical or mental development, but none the less composed of mind, body and soul. The affirmation of the last may be a matter of personal assumption, and for centuries has been considered to lie in the domain of the theologian, but every observant practitioner who is not too materially minded—and your true physician is not—has often been struck by some intangible, indefinable quality of the human that can be explained only very imperfectly by the mechanistic facts and theories of either psychology or physiology.

These few introductory remarks may appear, at first sight, to have little bearing on that ever-increasing complaint—backache. Let us therefore enumerate some of its causes—not necessarily in order of incidental frequency: (i) trauma, including muscle and ligamentous strain; (ii) spondylitis—osteoarthritic, ankylopoietic and tuberculous, and *spondylitis muscularis* (of Knaggs); (iii) ruptured intervertebral disk; (iv) uterine displacements, menstrual dysfunction and ovaritis; (v) so-called fibrositis; (vi) renal disease; (vii) *coitus interruptus*; (viii) neoplasm of the cord; (ix) emotional tension—that is, psychogenic determinants; (x) faulty posture—for example, flat feet, *hallux rigidus, et cetera.* Of these I am concerned chiefly with traumatic fibrositis, emotional tension and osteoarthritic spondylitis or syondylosis. That, I believe, is the usual apparent order of sequence; but the emotional tension may well in many instances precede the others.

In nearly every personal history out of many hundreds thoroughly investigated, I have found two almost invariable components—a past injury or strain of the back, possibly fifteen to twenty years previously, and a record of emotional tension or discontent. The latter is frequently an admission which most patients are reluctant to make, and rarely will make on first consultation. It is a time-worn although under-estimated adage that mind makes body, from the days of Cleobolus, who in 600 B.C. advised keeping a healthy mind in a healthy body, to the Freudian psychoanalysts of this century with their concept of the psychogenesis of somatic disease. We all know that a consciously worried man may very well become a sick man; but we do not so generally appreciate that an unconsciously or subconsciously worried or discontented man with no emotional gratification or outlet may become, with surprising rapidity, an equally ailing individual. If emotional disturbance, with the passage of time, can cause definite metabolic and tissue changes to appear in the organ or bodily area selected by the unconscious, then it would seem reasonable to infer that this choice could be predetermined in part by a previously existing trauma of that organ.

From the symbolic as well as from the physical point of view the back is a very significant area. The anatomy of the spine is that of an intricately elaborated structure, which in the course of human evolution has probably altered considerably according to the stresses and strains it has had to endure. It is the support of the trunk and head, enables us to maintain an upright posture, carries loads, physically and metaphorically, and in the unconscious mind is a vulnerable region, being symbolically the recipient of burdens and of attack from the rear.

To digress for a moment. You all know that the spinal column is composed of 24 vertebræ, the sacrum and the coccyx. The cord emits through the intervertebral foramina 32 pairs of nerves, which are delicately linked with the autonomic, sympathetic and parasympathetic systems. Half a dozen spinal ligaments support the structure, which is largely maintained and moved by a complex group of eight deep muscles covered by the lumbo-dorsal fascia.

This is a rough outline of the somewhat formidable system which is, in modern times, apparently so prone to disturbance of sensation and movement. As I have just mentioned, the back is subject to strong psychological affect. The popular expressions—someone or something is a "pain in the neck", "stabbed in the back", "spineless", "no back-bone", "turn my back on him", "when my back is turned", "my aching back", and the army phrase "so-and-so is 'always on my back'"—all lend support to this view. The pain and disability which ensue from emotional conflict and which are termed psychogenetic or psychosomatic, should not be dismissed lightly as "imagination"

FIGURE I.
Wilde pyretic couch (modified).

—a designation which not only expresses a lack of understanding on the part of the physician, but is a source of irritation to the patient and an implication of his dishonesty. Psychogenetic pain in the back may arise from an unsuspected and latent anxiety neurosis, which may embody repressed homosexuality and repressed feelings of hostility and aggression, supplemented in turn by those of guilt. This state of emotional conflict and tension, albeit below the surface, as it were, if of sufficient intensity and continued long enough, and especially if superimposed on a previously strained or debilitated or psychologically termed "gratification" organ, will eventually produce probably tissue metabolic disturbance and certainly pain and dysfunction. It is for this reason that many sufferers from backache may be said to be neurotics. The neuritic is often the neurotic. And, lest you may think that the term neurotic is a slur, let me add that it is extremely doubtful if any of us are really emotionally tranquil and undisturbed. In passing, it would be most interesting if some biochemist were to investigate the chemical tissue changes that might arise as a result of anxiety, discontent or depression. The pathology of boredom, for example, might well be a novel field of research.

In any case, it is most important to investigate and treat backache from the aspect of nervous tension. It is, to my mind, the keynote of success, for I am firmly convinced that emotional tension precedes tissue tension, which with regard to the back implies tension of muscles and ligaments, with accompanying spasm and resulting diminution of circulation and oxidation. In short, mental tension means muscle tension.

Treatment.

Examination.

Every patient is fully undressed and given a thorough physical examination, literally from head to foot. Laboratory aid is enlisted when necessary—blood counts, erythrocyte sedimentation rate, blood uric acid content, basal metabolic rate, Wassermann reaction, *et cetera.*

X-Ray Examination.

All patients during the past twenty years have had full X-ray examination of the spine and other affected joints. Doubtful teeth are also radiologically examined, although little belief is held in the toxic theory, unless gross sepsis is present.

Heat.

The Wilde pyretic couch has been used in one or other form since 1926, and more recently, whilst retaining the original principle, I have altered it and I hope carried out some improvements. Although I am aware that this

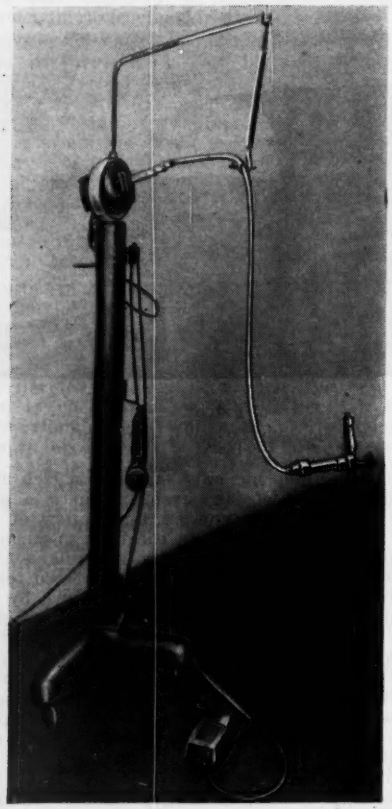

FIGURE II.
Johannsen electric vibrator (Frazer's modification).

couch once fell into some disfavour, owing largely to extravagant claims made for it, I am satisfied that this appliance is still the best and most natural method of applying moist heat to the whole body. Its use, however, is time-consuming.

Massage.

General hand massage, whilst soothing to the nerves and stimulating to the tissues, has little or no effect on backache, unless carried out with painful intensity. In my own practice an improved Johansen electric vibrator is used. This is the most powerful and penetrating of all vibrators and consists of a one-third horse-power motor delivering through a flexible shaft 3000 percussions per minute. I have redesigned the machine to allow of five speeds and five intensities of percussion.

Extension.

Extension or traction of the cervical part of the spine by means of a neck sling is well known to you. Generally, the patient is raised clear of the ground. For extension

FIGURE III.
Johannsen vibrator-spinal massage.

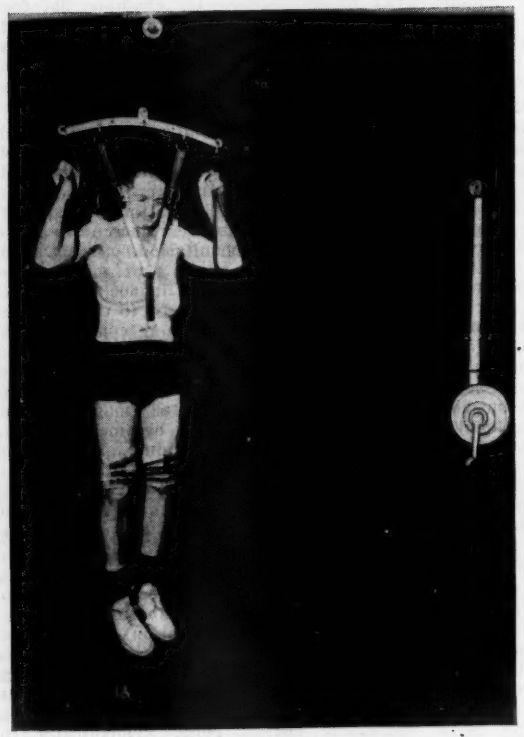

FIGURE IV.
Traction apparatus (Frazer).

of the lower dorsal and lumbar segments a corset is fitted, also knee gaiters, which are attached to ankle gaiters. The latter are adjusted to tested tension springs. By this means,

in addition to the weight of the patient's legs, an extra graduated pull up to 420 pounds can be applied.

Manipulation.

Manipulation is carried out frequently in suitable cases. An anæsthetic is employed when necessary.

Medication.

Sedation is emphasized. Early hours of sleep are essential. The old belief that the hours of sleep before midnight are more valuable than those after is borne out by experience. It is not the quantity of sleep that counts, but the quality of the rest obtained. Patients are asked to sleep on a hard bed or on an inner-spring mattress placed on a wooden platform. The height of the pillow is a factor in lessening stiffness of the neck in the morning. It has never been found necessary to admit any patient to hospital for the purpose of bed rest. Calcium in large doses has been used for years. Curare, "Prostigmin" and "Myanesin" are administered at times to relieve muscle spasm. The first-named would seem to be the most effective. The watery solution is preferred, but all have only a transient effect. Phenobarbital is not employed. Bromides and belladonna give better response. Gold, sulphonamides and streptomycin are without appreciable effect in backache.

FIGURE V.
Cervical portion of spine before traction.

Œstrogens are administered freely when indicated, and thyreoid for obesity, but under close observation. No noticeable benefit has been observed in backache from the desoxycorticosterone-vitamin *C* combination. Stilbœstrol is not employed.

Vitamins have been greatly prescribed in the past, as far as possible by injection, but it would seem that no outstanding results accrue from the exhibition, even in large doses, of any single vitamin, although they are of great value in building up general health.

FIGURE VI.
Traction of cervical portion of spine—patient suspended by head. Approximately fifteen minutes after injection of "Myanesin".

Psychotherapy.

In the belief that repressed emotions have a profound bearing upon nervous and physical tension, every effort is directed towards resolving existing unconscious conflicts. A gradual approach is made to ascertain, in the light of psychoanalytic findings, both conscious and unconscious reactions to past history and present environment. Needless to say, this is the most difficult part of the treatment.

Shock Therapy.

In conjunction with the foregoing, and with a view to improving the nervous imbalance as well as extending and subsequently relaxing spinal muscles and ligaments, shock therapy is occasionally practised. Therapy takes place in the surgery and a mild shock is induced by the intravenous injection of "Aneuxol". A feeling of euphoria and ease of tension—mental and physical—is a frequent result.

Exercise.

Every patient is instructed to carry out five minutes' simple exercise each day. The method suggested is that of the Danish lieutenant, the late J. P. Müller, entitled "My System". This is followed by a five-minute hot shower and a brief cold shower. Experience over many years on one of the Barrier Reef islands has demonstrated the extreme value of exercises carried out in warm sea water, accompanied by graduated sunbathing and complete bodily inunction with shark-liver oil.

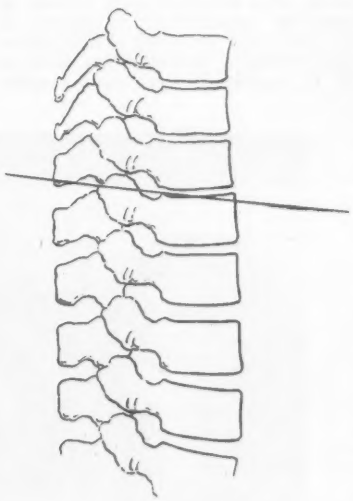

FIGURE VII.
Lumbar portion of spine during traction of approximately 200 pounds *plus* the weight of the lower limbs. Ten minutes after injection of "Myanesin". (No traction exerted above transverse line.)

Diet.

No special diet is recommended, save that meat should be undercooked and in lard or butter (mixed and stale dripping being difficult of digestion). Pastries should be avoided and vegetables and fruits not stored in a refrigerator. In cases of severe constipation and dyschezia, colonic (Plombières) lavage is advised.

No restrictions are placed on the moderate use of alcohol, if it is of first quality, except that indulgence in fortified sweet wines is not beneficial. A whisky and soda or a glass of Burgundy or claret (of which Australia can produce some very good types) is to be recommended. Temperate smoking of good tobacco—if such a thing is obtainable nowadays—can do no harm.

Conclusion.

It can be seen from the foregoing that the treatment of backache, although at first sight apparently simple, is by no means invariably so. It is actually a strenuous and a full-time specialty. All these cases from which experience has been drawn have been encountered in private practice, and most of them have been of the chronic and refractory type. Few of the patients have been treated at first hand; many have been treated previously by from three to thirty practitioners.

The method outlined above, which has been employed for many years, gives satisfactory results in 80% to 90% of cases of backache. There are, of course, always the individuals who are too abnormal for treatment, and those who really "enjoy bad health"—the psycho-pathological variety. As with other forms of the rheumatic syndrome, diathesis is regarded as of supreme importance, and too much stress cannot be laid upon the necessity for early—and very early—treatment.

Acknowledgements.

My thanks are due to the late Dr. Paul Tillett, to his able technician, Miss Dalgleish, and to Mr. Charles W. Phillips, Mr. Cyrus Quinn, and Messrs. Richard Wildridge and Company, engineers, Sydney, for their suggestions and assistance with regard to the traction apparatus.

Reports of Cases.

KRUKENBERG TUMOURS OF BOTH OVARIES SECONDARY TO CARCINOMA OF THE STOMACH.

By PHILIP C. THOMAS, M.R.C.O.G.,
Perth.

A KRUKENBERG TUMOUR has been defined by R. A. Willis as "a diffusely infiltrating, often bilateral, solid tumour of the ovaries, of myxomatous appearance, consisting of mucus-containing signet ring cells scattered amidst abundant œdematous ovarian stroma". However, the term is often loosely employed to include all secondary ovarian tumours except those originating from the uterus and Fallopian tubes.

The case recorded below is an example of this interesting condition.

Clinical Record.

The patient is a married woman, aged forty-two years, with two children, aged sixteen and six years respectively. She gave a history of "indigestion" for four years, with remissions lasting up to six months. This consisted of epigastric pain coming on immediately after meals and relieved by vomiting. There had been a rapid loss of about a stone in weight in the month prior to her admission to hospital. Menstruation had been normal up till twelve months previously, but during the past year epimenorrhagia had been present. She presented herself in April, 1950, with a hard, irregular-shaped mass rising out of the pelvis to the level of the costal margins, and the first provisional diagnosis made was that of uterine fibroid tumours. The hæmoglobin value was 11·6 grammes *per centum*. Laparotomy was performed on May 11, 1950, and two solid ovarian tumours, together with the uterus, were removed. While the abdomen was open a surgical colleague (Dr. Ross Robinson) confirmed the presence of a stomach growth, and he removed this eighteen days later by subtotal gastrectomy (see Figures I and II). Convalescence after both operations was smooth, and the patient was discharged from hospital on June 14, 1950.

FIGURE I.
Uterus and bilateral ovarian tumours, showing cut surfaces and dermoid cyst in the centre of the right ovary.

Description of the Specimens.

The Stomach.—Midway between the cardia and pylorus there is a large, flat ulcer measuring seven centimetres by four centimetres. It has undermined edges and a firm, smooth floor. The mucosal folds radiate towards it. Several small lymph nodes are found in the serosa, invaded by tumour cells.

The Ovaries.—Both ovaries retain their shape, but are enlarged; the right ovary measures 18 centimetres by 13 centimetres by 8·0 centimetres, and the left ovary 14 centimetres by 11 centimetres by 8·0 centimetres. Both tumours are solid, with the exception of a large dermoid cyst within the right ovary, which measures 8·0 centimetres by 5·0 centimetres by 5·0 centimetres and contains sebaceous material, hair and cartilage. Examination of the cut surface of both tumours reveals a yellowish-white cortex of more compact tumour visible as a broad, wavy band at the periphery, and greyish coloration of the central areas.

Microscopic Examination.—In all sections from the stomach and both ovaries an adenocarcinoma is evident, originating from gastric mucosa, and all specimens showed typical signet-ring tumour cells. The wall of the dermoid cyst consists of tumour cells and dense fibrous tissue.

Discussion.

Apart from spread from the uterus and Fallopian tubes, secondary carcinoma of the ovary may come from a primary growth in the gastro-intestinal tract, especially the pylorus, but sometimes from the colon, sigmoid colon, rectum, small intestine, gall-bladder, liver or pancreas, and very occasionally from the breast. Typically, the secondary ovarian growths in this latter group are of variable size, usually bilateral (90%), solid and with a lobulated nodular appearance, retaining the general shape of the ovary and showing no tendency to become adherent to surrounding structures. Ascites is frequent but not typical, and apart from secondary deposits in the perigastric lymph glands and sometimes in the peritoneum, Krukenberg tumours are often unaccompanied by metastases in other organs. Especially notable, as in this case, is the frequent escape of the liver.

The primary growth is often small and relatively symptomless, the large ovarian tumours producing, as exemplified in this case, the first or main signs of disease, and even at autopsy a small diffuse primary tumour may escape detection. This brings up the question of whether, in rare instances, Krukenberg tumours may be primary, and although Willis definitely refutes this possibility, Novak admits it. The route of dissemination of metastases from the primary growth to the ovaries has provided a controversial subject. Novak inclines to retrograde lymphatic spread for the majority, but admits that some may be blood-borne. On the other hand, Willis favours the transperitoneal route.

Conclusion.

This case illustrates two important points to be borne in mind when one is dealing with gastric and ovarian malignant disease. These are as follows.

1. In every case in which carcinoma of the ovary is suspected a routine pre-operative gastro-intestinal survey should be made to determine the possibility of a primary source of the tumour in the digestive tract. If this survey is inadvertently omitted, it should be made after operation.

2. Careful pelvic examination is necessary for any female patient presenting gastro-intestinal, and particularly gastric, symptoms.

FIGURE II.

Removed portion of stomach, showing a large carcinomatous ulcer.

Acknowledgements.

I wish to acknowledge help given by Dr. T. R. Lubbe in reporting on the tumours, and to thank Dr. Ross Robinson for his surgical collaboration.

Reviews.

METHODS IN MEDICAL RESEARCH.

THE occurrence of epidemics of disease has always caused great concern to man. It may be that from time to time more virulent strains of bacteria appear and take root in a vulnerable population. With this in mind it is of considerable interest, and indeed comforting, to learn that scientists are now making a detailed study of the factors which may bring about bacterial variants. In the most recently published volume[1] (Volume III) of "Methods in Medical Research" may be found a chapter, "Genetics of Micro-organisms", which will make most interesting reading. S. E. Luria states in his introduction to this chapter: "It may seem surprising that a section on genetics of micro-organisms should appear in Methods of Medical Research. The most obvious rationale for this inclusion is the importance of variation in the characteristics of the parasites for the pathology and epidemiology of infectious diseases. . . . For bacteria, the methods discussed cover 2 topics: the mutations affecting resistance to destructive agents, and the mutations recognizable by nutritional studies (commonly, if improperly, called 'nutritional' or 'biochemical' mutations). . . . The genetics of molds is represented by a discussion of methods in the genetics of the ascomycete Neurospora, a genus that already ranges with Drosophila and maize among the classic materials of genetic investigation."

Other chapters in this excellent volume, which is a worthy successor to Volumes I and II, discuss "Assay of Neurohumors" (associate editor, J. H. Gaddum), "Selected Psychomotor Measurement Methods" (associate editor, Walter R. Miles) and "Methods for Study of Peptide Structure" (associate editor, Choh Hao Li). Most of the writers of sections are carrying out their researches in America, but it is pleasing to note that in the chapter "Synthesis of Acetylcholine" the editors have chosen Dr. W. Feldberg, who is well known to many Australians for his work with C. H. Kellaway in Melbourne and who is now at the National Institute for Medical Research, London. Once more we can highly commend this volume to all those interested in medical science and research.

[1] "Methods in Medical Research"; Editor-in-Chief, Ralph W. Gerard; Volume III; 1950. Chicago: The Year Book Publishers, Incorporated. 8½" × 5½", pp. 340, with a few illustrations. Price: $7.00.

AN ANCIENT CHINESE MEDICAL MANUSCRIPT.

A HANDSOME BOOK has been published in Baltimore to perpetuate the unusual achievement of Ilza Veith, M.A., Ph.D., Lecturer on the History of Medicine in the University of Chicago, in translating from the Chinese language into fluent English one of the most ancient and important medical treatises to originate in eastern Asia. The translation of "Huang Ti Nei Ching Su Wên" or "The Yellow Emperor's Classic of Internal Medicine" takes up the latter half of the book and consists of 34 chapters which are thought to contain most of the basic ideas found in the complete text.

One gathers that the ancient work may have been written somewhere between the second and third centuries B.C., and that the modern edition (from which the recent translations have been taken) is from a printed volume known as the "Collection of the Four Imperial Libraries", published under the authority of the Chinese Government, 1772-1790. Many of the difficulties in the western interpretation of ancient oriental characters and ideologies had been previously overcome by the labours of a scientific chemist, Mr. Jacob W. Lindau, who set himself the tremendous task of translating the complete text in the early part of the present century. Dr. Henry E. Sigerist, at whose instigation the new translation was undertaken, has written an informative foreword in which he points out the value of such scholarly achievements to every student of medical history and Chinese culture in helping towards a better understanding of civilizations of the past.

The first part of the book is taken up with an analysis of the ancient text, and in a lengthy introduction Dr. Ilza Veith discusses such mystical conceptions as the five primary elements—water, fire, metal, wood and earth; the potent influences of the four seasons, the heavenly bodies, and the interactions of Yin and Yang in regulating human affairs; the technical refinements necessary for the therapeutic procedures of acupuncture and moxibustion; and the philosophical and religious precepts of Taoism which seem to pervade the whole theory of health and disease, while at the same time indicating a way of life to be followed by the individual both in this world and in the next.

Most of the illustrations, inserted to assist the author's introductory explanations, are taken from the oriental collection of the late Dr. Howard Kelly in the Institute of the History of Medicine at the Johns Hopkins University; and they might be intelligible to a literate Chinese. Medical practitioners interested in medical history and philosophy of the ancients will find "The Yellow Emperor's Classic of Internal Medicine" a mine of information but not particularly entertaining.

THE BIOLOGY OF HUMAN STARVATION.

WHEN on the collapse of Germany and Japan those prisoners of war who had survived the semi-starvation and other inhuman treatment were liberated and introduced once more to civilized life with adequate food, the doctors directing the rehabilitation found to their regret and dismay that the problems presented had never been studied by them either in systematic treatises or through clinical experience. They had to feel their way in a medical territory which was only partly explored and they early discovered that the psychological aspects were actually greater than the physiological and pathological. The same difficulties were encountered when western Holland was released from the fury of the Teuton with this addition, that both sexes and all ages were

[1] "Huang Ti Nei Ching Su Wên: The Yellow Emperor's Classic of Internal Medicine", by I. Veith, M.A., Ph.D.; Chapters 1 to 34 translated from the Chinese with an introductory study; 1949. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson. 10" × 6¾", pp. 280, with illustrations. Price: 5s.

in the same distressing condition. The Minnesota Laboratory of Physiological Hygiene undertook a detailed and protracted inquiry into the whole matter with organization and team work which, one may venture to assert, have never been equalled. The main conclusions of this investigation were presented in the American journal *Science* of August 25, 1950, and this article formed the basis of an editorial in THE MEDICAL JOURNAL OF AUSTRALIA of December 5, 1950. Now in two heavy volumes we have the full detail of this laborious research.[1] Thirty-two conscientious objectors were voluntarily kept for a year under investigation; for the first three months the diet was ample, then came six months at 1570 kilo-calories a day with only a few grammes of animal protein a week, then came finally three months' rehabilitation on a rich ration. That the undernutrition was very real and not tempered by humanitarian intrusion is shown by a photo of some of the voluntary victims having a sun bath and displaying a pathetic emaciation. A generous tribute of praise must be proffered to these steadfast young men. It may be briefly stated that every device for investigating the whole and every part of the human body was brought into operation and was placed in expert hands. In addition, trained psychiatrists closely investigated the behaviour problems during starvation and rehabilitation and these turned out to be of major importance.

Certain experiments on semi-starvation had been carried out before, but with nothing like the thoroughness of the Minnesota inquiry; these are mentioned and due recognition of their value is paid. Some qualifications of earlier conclusions became necessary; the heart, for example, was found to lose substance to a recognizable degree whilst the brain, hitherto regarded as immune from surrender of substance, was proved in animal experiment to undergo some loss of neural matter with a corresponding increase of fluid. A very important find was that every effort of the body is made to keep the circulating plasma protein level constant; when in extreme starvation this level cannot be maintained a dangerous condition arises with œdema, polyuria, bradycardia and extreme weakness. When all is so excellent it is difficult to single out special portions for praise, but it may be mentioned that the chapters on nutrition, on metabolism, general and special, and on psychology are of outstanding merit. The Minnesota experiment will, in the words of Sir Jack Drummond, "become a classic from the day it is published". Should another world war arise—*procul omen abesto!*—and should there be survivors, medical science will know what to expect in the starved and how best to remedy the condition. For this not only the members of the medical profession, but the whole world should be grateful.

A YEAR BOOK OF UROLOGY.

UNHERALDED and with no perceptible ruffling of the surface a change in editorship appears in "The 1950 Year Book of Urology"; William Wallace Scott has taken over from the editor for many previous years, Oswald S. Lowsley.[2] The new editor has had the task of presenting, as in all this year's Year Books, a review of his subject for the past ten years. It is interesting to note that, as in most other fields of medicine and surgery, the innovations and developments of the period are overshadowed by the introduction of the antibiotics and advances in endocrinology. It is also obvious, both from the introductory review and from the volume as a whole, that general considerations of physiology and pathology are being allowed an increasingly important place in this rather circumscribed surgical specialty. The journals abstracted are not only from a wide geographical field but also from a wide medical field, although surgical and urological publications are most prominent. The journals are those received by the editor between October, 1949, and October, 1950. The opening chapter on general considerations covers examination of the urine, infections, calculi, anæsthesia and urography (pyelography). In the chapter on the kidney are sections on anomalies, anatomy and physiology, tumours, tuberculosis, hæmaturia, trauma, renal insufficiency, miscellaneous subjects and surgical technique. The adrenals have a chapter to themselves this year, the main aspects included being adrenal cortical hyperfunction and tumours, especially phæochromocytoma. A short chapter on the ureter contains sections on anomalies, calculi and surgical technique. In the chapter on the bladder much the largest section deals with tumours, a fact presumably reflecting what the editor refers to as "the magnitude of the problem of bladder cancer"; the other sections are concerned with surgical technique, anomalies, micturition, neurogenic bladder, cystitis and urological problems in the female subject. The chapter on the prostate has sections on the choice of operative approach, transurethral resection, suprapubic, retrograde and perineal prostatectomy, carcinoma, and physiological and pathological studies. The last chapter, on the genitalia, deals with the penis, the urethra, hypospadias, testis tumours, scrotal swellings, the *vas deferens* and seminal vesicles, infertility and miscellaneous subjects. Australian authors mentioned include C. Craig, D. B. Duffy, K. B. Fraser, V. S. Howarth and R. J. Silverton. Good printing, binding and general presentation combine with the subject matter to make this an attractive and useful summary of current urological literature.

[1] "The Biology of Human Starvation", by A. Keys, J. Brozek, A. Henschel, O. Mickelsen and H. L. Taylor, with forewords by J. C. Drummond, R. M. Wilder, C. G. King and R. R. Williams; 1950. Minneapolis: The University of Minnesota Press. Melbourne: Geoffrey Cumberlege, Oxford University Press. 10″ × 7″. In two volumes. Volume I, pp. 790; Volume II, pp. 632. Both volumes contain illustrations. Price: £12 12s.

[2] "The 1950 Year Book of Urology (October, 1949-October, 1950)", edited by William Wallace Scott, M.D., Ph.D.; 1951. Chicago: The Year Book Publishers, Incorporated. 8″ × 5″, pp. 416. Price: $5.00.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"How Psychiatry Helps", by Phillip Polatin, M.D., and Ellen C. Philtine, with a foreword by Nolan D. C. Lewis, M.D.; 1951. Kingswood, Surrey: The World's Work Limited. 7½″ × 5″, pp. 262. Price: 10s. 6d.

A book for the non-medical reader explaining what mental illnesses are and how they are treated.

"Eyes in Industry: A Comprehensive Book on Eyesight Written for Industrial Workers", by Dorothy Adams Campbell, M.A., M.B., B.S., W. J. B. Riddell, M.D., F.R.S.E., F.R.F.P.S., Sir Arthur Salusbury MacNalty, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S., Hon. F.R.S.E., with a preface by The Lord McGowan, K.B.E., D.C.L., LL.D., and an introduction by Sir Stewart Duke-Elder, K.C.V.O., D.Sc., Ph.D., M.D., F.R.C.S.; 1951. London: Longmans, Green and Company. 10″ × 7″, pp. 250, with 26 plates, some in colour. Price: 49s. 6d.

Written in order to stimulate the interest of the worker in industry in the preservation of his eyesight.

"Cytology and Cell Physiology", edited by Geoffrey H. Bourne; Second Edition; 1951. Oxford: Geoffrey Cumberlege, The Clarendon Press. 9½″ × 6″, pp. 540, with 33 plates and many text figures. Price: 87s. 6d.

An attempt is made to bring together chemical, physico-chemical and morphological aspects of the study of cells in a number of subjects which are representative of different fields of study of cells.

"A Text-Book of X-Ray Diagnosis by British Authors", in four volumes, edited by S. Cochrane Shanks, M.D., F.R.C.P., F.F.R., and Peter Kerley, M.D., F.R.C.P., F.F.R., D.M.R.E.; Second Edition, Volume I; 1951. London: H. K. Lewis and Company, Limited. 9½″ × 6½″, pp. 448, with 439 illustrations. Price: 45s.

This volume deals with the central nervous system, the teeth and jaws, the eye, the accessory nasal sinuses, and the ear and temporal bone.

"Atlas of Histologic Diagnosis in Surgical Pathology", by Karl T. Neubuerger, M.D., with a section on Exfoliative Cytology by Walter T. Wikle, B.S., M.S., M.D.; 1951. Baltimore: The Williams and Wilkins Company; Sydney: Angus and Robertson, Limited. 10″ × 7″, pp. 470, with 880 photographs. Price: £5 18s. 3d.

Designed to meet the needs of senior students, resident medical officers and practitioners in the making of histopathological diagnoses of surgical specimens and biopsies.

"Brain Metabolism and Cerebral Disorders", by Harold E. Himwich, M.D.; 1951. Baltimore: The Williams and Wilkins Company; Sydney: Angus and Robertson, Limited. 9″ × 6″, pp. 462, with 52 illustrations. Price: £3 4s. 6d.

Deals with cellular physiology, the quantitation of the metabolic rate of the brain *in vivo* and the application of fundamental data to disease.

The Medical Journal of Australia

SATURDAY, MAY 26, 1951.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

DETECTION OF THE UNRECOGNIZED DIABETIC.

THE Diabetes Detection Drive started by the American Diabetes Association in December, 1948, is now fairly well known. It is based on the finding from various local investigations that for every known diabetic there appears to be one with unrecognized disease; the object is to find the unrecognized diabetics in the United States, whose number is regarded as approximately one million. The advantages of this to both individual and nation need no elaboration to medical readers, and the desirability of some such procedure in Australia was suggested in these columns as long ago as September 10, 1949. In a discussion on diabetes at the Australasian Medical Congress (British Medical Association) in Brisbane last year,[1] Kempson Maddox expressed the view that if part of the next census was devoted to questions about chronic disease, and if the health of a sample of the community was surveyed by a national agency, it would probably be found, as in the United States, that an undiscovered diabetic existed for each known diabetic. He also remarked that so far as one could tell, the over-all problem of diabetes in Australia was no less than in any other prosperous country; and yet its importance and the care of diabetics did not appear to have impinged at all upon the public health authorities of Australia and New Zealand. H. O. Lancaster read a paper (which was later published[2]) on diabetic prevalence in New South Wales, as part of the symposium opening the discussion; in this he presented evidence to show that the prevalence in New South Wales may be somewhat less than that in the United States, but it is sufficiently high to be taken seriously. Apparently the position in the United States has been taken seriously in many quarters, and the Diabetes Detection Drive, which has the endorsement of the American Medical Association, has made some progress. An interesting example of its operation has been described by T. P. Sharkey *et alii* in an account of a drive in Dayton, Ohio.[1] The drive was initiated and financed by the Montgomery County Medical Society and conducted as an official activity; apart from its value in detecting diabetics, it provides an excellent example of a vigorous public campaign conducted with efficiency and dignity, and also of a piece of public service rendered by the organized medical profession in such a way as to win public commendation. The object was not to have a brief campaign for a week or so, as has been done in some other places, but to maintain the drive continuously. Before it was launched, widespread community support was enlisted by publicity programmes involving newspapers, radio, television, industrial publications, parent-teacher organizations and civic agencies. The detailed account of this preliminary work makes interesting reading; although relating to conditions in an American city, it should be instructive to anyone concerned with the public relations of medicine and the medical profession. In most cases support was easily and quickly obtained. Conferences were held with editors and reporters of all the city's newspapers; questions of sceptical reporters looking for ulterior motives in the campaign were answered "fully and amiably", and unanimous approval of the programme was given by all when the newspaper staffs found that the members of the medical profession were trying to do something constructive for the community free of charge and without asking for contributions of funds. The newspaper cooperation appears to have been satisfactory from the point of view not only of enthusiastic publicity, but also of quality of medical information given and observance of professional ethics. The results obtained from the drive itself indicate that the mass testing of school children and of industrial workers affords the simplest potential means for detecting unrecognized diabetes under controlled conditions in a large segment of the population. Of 38,528 children tested, 1867 (4·84%) had glycosuria; of these, 1022 had subsequent blood sugar determinations, and 18 previously unrecognized diabetics were discovered. Of 21,094 industrial workers tested, 757 (3·5%) had glycosuria; of these, 370 had subsequent blood sugar determinations, and 68 previously unrecognized diabetics were revealed. The relatively high incidence of glycosuria can be attributed to the fact that most of the tests were made postprandially, but Sharkey *et alii* point out that it is important to obtain blood sugar determinations on all patients with glycosuria, whether or not preceding or subsequent urine examination reveals sugar; the earliest cases of diabetes will be discovered by initial postprandial studies. Altogether, up to the time that this paper was written, 69,159 persons had been tested in Dayton, and 2991 (4·3%) had glycosuria. Of 2211 who had blood sugar determinations, 151 were known diabetics and 148 had previously unrecognized diabetes revealed. This over-all finding is strikingly in accordance with the original assumption on which the American Diabetes Association initiated its drive. It certainly vindicates the action of the Montgomery County Medical Society in carrying out the Dayton drive and should encourage others to follow suit.

Just who in Australia might follow suit is a matter for thought. Public health authorities, whether or not

[1] THE MEDICAL JOURNAL OF AUSTRALIA, July 22, 1950.
[2] *Ibidem*, January 20, 1951.

[1] *The Journal of the American Medical Association*, November 11, 1950.

they are interested in diabetes, may not feel that a drive along the American lines is in their province at present. The striking feature about the report from Dayton is that it reveals the organized medical profession accepting the responsibility and fulfilling it very well. There is much to be said for this. The vast majority of the medical profession will agree that detection of the unrecognized diabetic is highly desirable, and their cooperation in any campaign to that end can reasonably be assumed. In these facts alone there is sufficient ground to suggest that the British Medical Association, as representing the organized profession, might consider the matter as a scientific activity. But there is more to it than that. The members of the Diabetes Detection Committee appointed by the Montgomery County Medical Society to manage the drive (they were general practitioners all) had amongst their tasks the eliciting of the cooperation of the newspapers whose attitude was not known. Permission to speak to editors and staff was requested, and in all cases granted. Indeed the reception appears to have been quite favourable, but some of the reporters were sceptical, particularly wondering whether the programme was a scheme to counteract propaganda for socialized medicine. Questions were asked of this type: "What are the doctors getting out of this campaign?"; "Is this a scheme for the doctors to get more patients?"; "Is this a scheme to raise more funds?". There was no difficulty about answering these questions freely and frankly, and suspicion was turned to ardent support. The support primarily sought and found was for a measure entirely in the public interest. The goodwill gained by the organized profession was quite secondary, but by no means to be despised. It is a well-known fact that, in this country as in most others, many people view the organized medical profession with suspicion and even hostility, though such an attitude towards the individual doctor, especially the family doctor, is rare. A logical basis for this attitude is not easily found, but it is unfortunate to say the least. The Montgomery County Medical Society has shown a positive type of activity that could go far to dispel prejudice and misunderstanding. Perhaps the idea is one that the Federal Council of the British Medical Association in Australia might care to refer to the Branches for consideration.

Current Comment.

THE IMPORTANCE OF CONTROLS.

MOST medical investigators, perhaps all, will protest their regard for the use of controls in the evaluation of, for example, a new method of treatment. The ordinary practitioner who never has written, and does not anticipate that he ever will write, a paper for publication will stand with the experienced research worker and inveterate report-writer on this point. Yet a little consideration of the question quickly suggests that mere lip service to the principle is common. We all know and look down our noses at the patent medicine advertisement with its testimonials and the sweeping claims of the results obtained with one bottle of the nostrum. We can all quote adroitly and knowingly the old *post hoc ergo propter hoc* tag and even expound it. Yet the contributor to the medical discussion who tells us about his series of two cases is all too familiar, and it is not unknown for the writer of a paper intended for publication to include amongst his results a series of one case in which the desired result was obtained in this case and to claim a "100%" success. It certainly cannot be denied that conclusions are often drawn in practice and on paper from investigations in which adequate controls are neglected. Nevertheless, it is startling to learn what was found by O. B. Ross, junior,[1] from a review of 100 current articles appearing in five leading American medical periodicals. The articles dealt with some procedure or some form of therapy that was recommended or condemned. The journals were studied at random until 100 such articles were evaluated; there was no artificial selection and no exclusion. Ross found that in 45% of the articles there was no control in the investigation reported and in 18% there was inadequate control; in 27% the investigation was well controlled and in 10% control was impossible. A satisfactory control was defined as "a number of untreated patients, or procedures, approximately equal to the number treated". These were managed in exactly the same manner as those treated; the specific form of therapy being tested was the only variable factor. Without such control assessment of results is impossible or liable to fallacy, so that of this sample of current recommended therapy collected by Ross only 27% can unquestionably be shown to improve the natural course of the disorder. As Ross remarks, other therapy may well be beneficial, but "verification of its value is not apparent in the accurate and predictable method of science". He concedes, of course, that in certain circumstances controls are of less importance than in others. Forms of treatment used for diseases whose known courses are quite constant (for example, the virtual 100% mortality of rabies) require less rigid controls for evaluation. Even, however, the use of previously reported cases as controls for a subsequently treated group must be viewed critically when variable factors cannot be excluded. In most cases we just cannot be sure of results without adequate controls. Ross rightly emphasizes that the use of controls is not just a tool of highly specialized teachers or research men working with tremendous volumes of material. It is equally important to the ordinary practitioner of medicine who treats much smaller numbers of patients. To ignore this principle is to invite fallacy in the evaluation of therapeutic procedures. Naturally there will be instances in which small groups of unusual cases or isolated observations occur and will merit reporting, although careful control has not been possible. Similarly, the practitioner cannot be always thinking in terms of controls as he goes the round of his everyday practice. The essential point, however, is to evaluate the situation soundly and not to claim for uncontrolled results, whether in a paper for publication or in routine practice, a significance and a validity that they do not warrant. In general, a sceptical attitude should be maintained towards all therapy or procedures proposed as effective unless an adequate untreated parallel series is compared with the treated series.

HEXACHLOROPHENE AND THE SURGICAL SCRUB.

IN 1944 a report was published by E. F. Traub *et alii*[2] on the use of the synthetic germicide hexachlorophene, or G-11, for the reduction of the bacterial counts on the skin surface, especially on the hands in the "pre-operative scrub". Since then many others have confirmed their favourable findings, and the status of hexachlorophene has become well established. Most of the early investigators used liquid soap incorporating hexachlorophene, though use was made of bar soap by Traub and his colleagues and others. A recent report dealing with hexachlorophene in soap, by R. R. Best *et alii*,[3] makes special reference to bar

[1] *The Journal of the American Medical Association*, January 13, 1951.
[2] *Surgery, Gynecology and Obstetrics*, August, 1944.
[3] *Archives of Surgery*, November, 1950.

soap, pointing out that it is less irritating than liquid soap and more convenient for many purposes—for example, for use in the home and during travelling and in emergency stations and army field units. In experiments at the University Hospital, University of Nebraska Medical School, Best and his colleagues found that hexachlorophene incorporated in a bar soap reduced the bacterial flora of the skin more effectively than did ordinary bar soap; an alcoholic rinse reduced its effectiveness. As others have found, the cumulative factor and sustained action of hexachlorophene were important in maintaining a low skin level of bacterial flora, and it is recommended that hospital personnel, particularly those with operating room duties, should use the bar soap containing hexachlorophene in their daily toilet; for economy purposes liquid soap containing hexachlorophene is recommended for use in the operating theatre provided it is tolerated by the skin. Best *et alii* claim that the use of a bar soap containing hexachlorophene can materially reduce the time necessary for a surgical scrub and eliminate the scrubbing brush and the irritating alcoholic rinse. Three minutes are considered sufficient time, the nails being cleaned after one minute and scrubbing then continuing for two more minutes. This total scrubbing should be lengthened to five minutes if the soap is not used daily for scrubbing or in the daily toilet.

Another interesting development is the incorporation of hexachlorophene in a new skin detergent, pHisoderm This detergent, which is a mixture of sodium octylphenoxyethoxyethyl ether sulphonate, lanolin cholesterols and petrolatum, lowers the surface tension of water and is an active emulsifying agent; it is stated to be about 40% more active than regular soap as a cleansing agent. It is fortified with 3% of hexachlorophene. T. C. Chisholm *et alii*[1] report favourably on the combination and describe the pre-operative scrubbing technique which has been in use at the Peter Bent Brigham Hospital, Boston, for the past two years and has produced satisfactory results. A similar technique has proved satisfactory for obstetrical work at the Boston Lying-in-Hospital and the Free Hospital for Women, according to D. E. Reid, C. W. Walter and A. S. Buck,[2] the reduced scrubbing time being particularly valuable; obstetrical practice does not always allow time for the conventional surgical scrub, and there is a real danger that the nursing staff, with many duties to perform, will become lax in carrying out tedious hand preparation. The scrub procedure is briefly as follows, a "Nylon" bristle brush being used: those who scrub at intervals of three days or longer apply 30 brush strokes to the skin (systematically to cover all areas) and 50 to the nails (this requires about ten minutes); those who scrub every two days apply 15 strokes to the skin and 25 to the nails (this takes about five minutes); those who scrub daily and use pHisoderm with hexachlorophene for their routine handwashing apply nine strokes to each skin area and 15 to the finger nails (this takes about ninety seconds and is known as the "ninety second" scrub). The Peter Bent Brigham Hospital procedure is broadly similar to this, the only major difference being the additional and final step of rubbing the hands and arms while they are immersed in a 1: 1000 aqueous solution of "Zephiran" for two minutes. There appears to be little question of the effectiveness of these methods faithfully carried out, and the reduced scrubbing time is attractive. It is quite essential, however, for an effective short scrub that two conditions be observed: daily exposure to the detergent and a thorough anatomical (systematic) scrub. The essence of the method's effectiveness is the cumulative effect brought about by repeated and exclusive use of the one agent, and this is the main ground on which it has been criticized. I. H. Blank *et alii*[3] regard the procedure as impractical and likely to develop a false sense of security; confidence in a material known to be effective after repeated application may lead to unconscious dependence upon it for single use. This is surely a pessimistic view, but it cannot be dismissed. Blank and his colleagues propose a technique designed to "degerm" the skin with a single scrub, consisting of a two-minute soap and brush scrub, followed by a two-minute immersion in a solution of 0·1% hexachlorophene and 0·5% cetyl alcohol in 70% (by volume) of isopropyl alcohol. They produce results to support their method, in which, of course, the cumulative effect of hexachlorophene is maintained, though it is not depended upon. The cetyl alcohol serves as an emollient for the surgeon's skin. No doubt further techniques will be developed, as none of those yet described is perfect. The constant factor so far, and presumably the one likely to remain, is the germicide hexachlorophene.

[1] *Surgery*, November, 1950.
[2] *Surgery, Gynecology and Obstetrics*, November, 1950.
[3] *Ibidem.*

ORAL AND RECTAL TEMPERATURES IN MAN.

THE clinical thermometer is used freely by lay people as well as by medical practitioners, and its readings have been granted a certain authority out of proportion to their true significance. The reason behind this seems to follow the pattern, always potentially fallacious, attached to most special investigations; the readings are regarded as objective instrumental observations, able to stand in their own right, and less subject to human error than the results of direct examination of the patient with the eyes, ears or hands. The wise physician, of course, avoids this error, but it is remarkably easy to fall into, and most non-medical persons are caught in it. Its strength is greatly reinforced by the common practice of marking a "normal" level on the clinical thermometer. Many investigators have set out to determine a normal reading or a normal range of readings for oral or rectal temperatures; but their varied findings have added to the confusion. A paper by S. M. Horvath, H. Menduke and G. M. Piersol,[1] the publication of which was authorized by the Council on Physical Medicine and Rehabilitation of the American Medical Association, does something to settle the question, if only in a negative way. In it is described an investigation carried out on a group of healthy young men and women. Over a lengthy period their rectal and oral temperatures were recorded night and morning under standard conditions. The range of observations extended over a period of twenty-nine to one hundred and eighteen days for both male and female subjects. The total number of observations on 38 female subjects was 2810, a mean of 74 observations on each. The total number of observations on the 16 male subjects was 1248, a mean of 78 observations on each. The observations were subjected to rigorous statistical analysis. Certain main findings are of interest. Over a comparable period of twenty-nine days the mean morning rectal temperature of women (98·6° F.) was higher than that for men (98·2° F.), and as well, the variability in the mean values was greater for women than for men. The mean evening rectal temperature, which was the same for both men and women, had a significantly higher value in both cases than the mean morning rectal temperature. Another point that was made clear was that there is no single "normal" temperature value for all men, nor is there a single "normal range" of temperature for all men. These statements are equally true with respect to the differences between rectal and oral temperatures. In any specific person there was found to be no single constant rectal-oral difference over his range of body temperature. Thus the investigation leaves us without absolute standards and without hope of obtaining them, and it is well to learn the appropriate lesson from this. It is obvious, as Horvath, Menduke and Piersol point out, that a part of the difficulty associated with measurements of body temperature lies in the failure to appreciate that "normal" values for body temperature are merely vague statements of someone's average, and that a range of values is more significant. Worship of the thermometer with its arrow pointing to a fixed value is harmful. A thermometer can be of greater value if there is understanding of normal temperature variability and an appreciation of the fact that the shift of body temperature away from or back toward the normal

[1] *The Journal of the American Medical Association*, December 30, 1950.

range for the individual patient is significant rather than a single absolute value. It is interesting also in this regard to read a note on the rectal temperature of infants which was supplied in answer to a question.[1] Here again it is pointed out that there is probably no "normal" rectal temperature for infants aged one to twelve months, but rather that there are variable temperatures within the boundaries of normal. This is particularly so because of the instability of the heat-regulating system in the newborn. It is stated that if the bulb of the thermometer is inserted five centimetres into the rectum a higher temperature will be registered than if it is inserted only three centimetres. Factors particularly causing variation are bodily movements, ingestion of food and the external temperature. A lowering may result from lessened protection of the body or coolness of the environment, and a rise from bodily exercise, restlessness and crying. Some children have a constant rectal temperature somewhat higher than the normal average; these infants, it is said, are often members of neurotic families. The writer of the note concludes with the remark that oscillations in rectal temperature are so universal that they should be considered normal manifestations based on a somewhat unstable heat-regulating mechanism in young infants. He does not quote any figures, even those that might be regarded as the very broadest range of normality. It seems to be important to get right away from the idea of absolute values for the temperatures of either infants or adults, and to insist that the thermometer reading take its place alongside all the other information that we have about a particular individual in health and in illness.

DIABETIC RENAL DISEASE.

THE discovery and the use of insulin in the treatment of *diabetes mellitus* have, on the one hand, made possible the successful treatment of the disease and prolonged the lives of many thousands of persons. On the other hand, many diabetics who are successfully treated become affected by vascular changes and renal disease. Some observers have pointed out that whereas in former days large numbers of diabetics died in a state of coma, this cause of death is at the present time comparatively rare. C. J. Bjerkelund, in a recent article on diabetic renal disease,[2] writes that it seems increasingly probable that the so-called vascular complications of diabetes are in fact not complications, but part of the disease process itself.

Bjerkelund has carried out a study of 1335 diabetics, 602 males and 733 females, treated in the medical department of the University Hospital, Oslo, between the years 1930 and 1950. The patients were stabilized on diet and insulin. The principle adopted in diabetic treatment was the institution of a dietary *régime* with a small carbohydrate intake and a low total caloric value. The majority of the patients received from 150 to 200 grammes of carbohydrate a day, but allowances were made for the patients' work and total caloric requirements. The reduction in carbohydrate intake was achieved by prohibiting the ingestion of sugar and by rationing bread, potatoes and milk. It was found that renal disease occurred in 10% of the total, 9% of males and 12% of females. The incidence of renal disease increased considerably with the increasing duration of the diabetes. While only 3% of the males and 4·5% of the females manifested renal disease after periods of up to five years of diabetes, the corresponding figures for those who had suffered from diabetes for fifteen years or more were 32% and 31% respectively. The systolic and diastolic blood pressures of the diabetics without renal disease are compared with the pressures of those who suffered from renal changes. Both systolic and diastolic pressures were higher in the latter group than in the former. This was true for both males and females. The average difference in systolic pressure in males was about 26 millimetres of mercury, and this was uniform in all age groups. The difference in women was an average of 15 millimetres of mercury, but increased with increasing age. The average diastolic pressure was about 14 millimetres higher in the group with diabetic renal disease in both males and females, and this difference was fairly constant in all age groups. Retinopathy was found to affect chiefly those patients who suffered from renal disease; 68% of males and 80% of females in the group manifested changes in the retina. Retinopathy also increased considerably in frequency with the increase in the duration of the diabetes. In this series retinopathy was found in 29% of males and in 54% of females who had had the disease for fifteen years or more. Bjerkelund points out that retinopathy often begins before albuminuria can be demonstrated. He thinks that this indicates that retinopathy is a concomitant manifestation of the underlying pathological process; in this case it is the visual disturbance which leads the patient to seek medical advice. One of the author's conclusions is that as a rule persistent albuminuria in a diabetic which is not due to some coincidental complication always leads to renal insufficiency and uræmia provided the patient lives long enough.

In his general discussion Bjerkelund states that it is now well known that the degenerative vascular changes in diabetes involve in the most serious cases not only the arteries and the arterioles, but also the capillaries and veins. Ballantyne found by histological investigation that the small, circular, deep retinal hæmorrhages were often really microscopic aneurysms of the capillaries. In Bjerkelund's opinion it is reasonable to suppose a common pathological basis for all degenerative vascular changes in diabetes. So far no particular metabolic disturbance has been found responsible for the degenerative vascular changes. A good deal of work has been done on the relationship of persistent hypercholesterolæmia and the development of arteriosclerosis. It has been pointed out that diets with a high fat content which are often associated with a high blood cholesterol level tend to produce arteriosclerosis. With the introduction of a diet with a low fat and a high carbohydrate content a definite drop in the average of the blood cholesterol level has been noted. It is well known that diabetic acidosis and coma are accompanied by hyperlipæmia and fatty infiltration of the liver. Bjerkelund also refers to indications that the parenteral administration of insulin is not a complete substitute for the natural glandular secretions. He states that even in the most carefully controlled diabetes there will be in the twenty-four hours periods of relative excess or deficiency of insulin and that these periodical fluctuations will have a far-reaching effect on fat metabolism. Bjerkelund mentions findings by Rittenberg and Schoenheimer that the fatty tissue of the body is not a static, inactive tissue, as formerly supposed, but that fat is constantly undergoing exchange in the body. These experiments, he points out, have lent a new actuality to the question of the possible harmful effect of fat transport through the blood vessels, and hence to the related problem of how much harm can be produced by an increase of fat transport as the result of obesity and a diet with a high fat content. In Bjerkelund's investigations no support for these views was forthcoming. No general increase in body weight was found in patients with diabetic renal disease, nor was any difference found in the blood cholesterol levels of patients with and of those without renal disease. It is of course possible, as Bjerkelund points out, that among other circumstances which might conceivably predispose to vascular complications in diabetes is the possibility that the destruction of the islets of Langerhans or other parts of the pancreas leads to other hormonal disturbances besides lack of insulin. As indicating the urgent need for research in the investigation of diabetes and also of arteriosclerosis, Bjerkelund refers to the treatment of diabetes and how it may be so arranged that retinopathy and renal disease can be avoided, pointing out that there is no general agreement on the matter. In his series the control of patients has not been sufficiently

[1] *The Journal of the American Medical Association*, December 16, 1950.

[2] *Acta medica Scandinavica*, Volume CXXXIX, Number 2, 1951.

regular and uniform to allow of any conclusions being drawn. Perusal of the literature does not reveal any general agreement on the matter. Some authors have claimed to find a correlation between the frequency of coma and that of vascular complications, but others have denied this. Joslin has laid stress on the control of diabetes and has expressed the opinion that poor control is a predisposing cause of arteriosclerosis. Bjerkelund also refers to the findings of Priscilla White that 8% of juvenile diabetics whom she found free from vascular complications after twenty years of the disease were amongst the most carefully controlled. On the other hand, Dolger carried out observations on 200 young diabetics who were carefully examined at monthly intervals for periods up to 25 years. It was found that the time of development of retinopathy and its severity were strictly comparable in well and poorly controlled diabetics.

In any discussion on renal diabetes reference should be made to the "intercapillary glomerulosclerosis" described by Kimmelstiel and Wilson in 1936, and probably peculiar to diabetes. Admittedly Bjerkelund is not particularly interested in the pathological side of his subject; but, in order that readers may obtain a balanced view of the condition, they are referred to an article by Ian Gilliland, appearing in the *British Medical Journal* of April 28, 1951. Gilliland writes on the subject of the Kimmelstiel-Wilson lesion and holds that it is capable of clinical recognition.

THE MANAGEMENT OF SEVERE GASTRO-DUODENAL HÆMORRHAGE.

THE long-standing dispute on the relative merits of medical and surgical treatment of gastro-duodenal hæmorrhage has little to justify it. It apparently arises, as John D. Stewart points out,[1] from a yearning for standardization, for conformity to the Procrustean bed. The two forms of treatment must both be conceded to have merits, but merits relative not so much to one another as to the patient and his condition and to the medical attendant and his facilities. There is mounting evidence, Stewart claims, that a patient with exsanguinating duodenal or gastric ulcer can be successfully treated by immediate restoration of hæmoglobin values and surgical prevention of further bleeding by means of subtotal gastrectomy. He quotes results from a series of 40 cases to support the value of this method; yet—and this is noteworthy—he does not recommend the method for general adoption. Necessary to its success, he states, are resident and laboratory teams available round the clock and eagerly interested in the programme, a blood bank with large and fluid assets, anæsthesia facilities of a high order, and a surgeon with considerable experience in difficult gastric surgery, as well as a willingness to work at night and to sacrifice the day's routine. This exacting standard explains why Stewart limits the method's application, though it must be remembered that many of the requirements are equally essential for successful medical treatment—notably facilities for extensive blood transfusion and constant attention by medical and nursing staff. In a series of three papers read at the annual session of the American Medical Association last year and in the account of the discussion that followed,[2] much support may be found for medical treatment, though no attempt is made to underrate the value of surgical treatment in suitable circumstances. In their paper W. F. Lipp, M. H. Lipsitz, E. Milch and A. H. Aaron describe the results obtained in 101 cases of massive hæmorrhage drawn from 274 cases of bleeding peptic ulcer of varying degrees. Massive hæmorrhage is defined as "massive continuous bleeding with an exhibition of the classic picture of collapse: pallor, sweating, air hunger, hypotension, tachycardia, acute anemia, reduced hematocrit and diminished blood volume". The general conclusion reached is that in the majority of cases this usually critical state will respond to intensive medical treatment consisting of the administration of massive and continuous multiple blood transfusions, oxygen and opiates, that in a certain small group of cases surgical intervention with gastric resection will be required, and that members of this group can be fairly readily determined through their failure to respond to transfusion. A description is given of what is called the "test of transfusion" and how this may be interpreted with a view to surgical intervention or otherwise. The test requires immediate multiple transfusions, as much as 2000 millilitres of blood being given in an hour. If after three hours appreciable clinical improvement has not occurred, immediate operative intervention is considered necessary; if clinical improvement has occurred, the treatment is continued. At the end of six hours blood replacement is ceased, and the patient is watched. Recurrence of massive hæmorrhage is the signal for further transfusion and immediate surgical operation. In its absence, medical treatment is continued. One criticism likely to be levelled at this test is that it involves immediate massive transfusion—a practice strongly opposed by many. In another paper of this group, dealing with the role of blood transfusions in the management of gastric hæmorrhage, H. M. Pollard and A. Wollum outline the objections raised to the liberal use of transfusions and agree that the cautious withholding of blood transfusions during the first few hours after the onset of hæmorrhage (unless shock occurs) may favour clot formation and cessation of bleeding. After that they favour transfusions and point out that many of the earlier objections can be related to faults of technique that no longer obtain; indeed, with the introduction of slow drip transfusion and improved methods of blood typing, the increased safety of blood transfusion has led to more frequent use of transfusion therapy in general. Here transfusion is indicated for control of shock and for prevention of harmful effects of anoxæmia on vital organs; the level at which the hæmoglobin value must be maintained if continuing or recurrent hæmorrhage is not to threaten life is set down at 50%. Pollard and Wollum offer as pointers to potential candidates for surgical intervention prognostic factors that in the past have been associated with high mortality rates. These include an age of over forty-five years, a first hæmorrhage, hæmatemesis, hæmorrhage persisting over twenty-four hours after the patient's admission to hospital or recurrent hæmorrhage, hæmorrhage occurring when the patient is following a full medical ulcer regimen, and coexisting complicating disease; liberal transfusion is particularly indicated for such patients, they state, in order "to keep them good operative risks". This is, of course, a list of wide scope, and most of the patients concerned should not go beyond the "potential" stage of surgical candidature.

Another factor that may complicate a decision on surgical intervention is the absence of an exact diagnosis. It may be thought that here the value of exploratory laparotomy would add considerably to the indications for intervention, but this is not the impression left in the third paper of the series, in which I. R. Jankelson and L. R. Milner deal particularly with hæmorrhage of undetermined origin. Jankelson and Milner found that exploratory laparotomy failed to reveal the cause in an appreciable number of cases, and they state that the diagnosis can be made nearly as often without as with exploration; in certain instances, however, exploration has proved the only means of making a definitive diagnosis. They favour medical management of patients during and after a single massive upper digestive tract hæmorrhage of undetermined origin, and surgical exploration if the patient has had repeated hæmorrhages. None of these papers provides any simple rule of thumb, acceptable without reservations, by which candidates for medical and surgical treatment can be selected, and the opinions expressed in them will not be acceptable to everyone. They do, however, contain much information and thoughtful comment that will help or at the least stimulate the thought of those who have to make these decisions.

[1] *Surgery*, October, 1950.

[2] *The Journal of the American Medical Association*, January 6, 1951.

Abstracts from Medical Literature.

THERAPEUTICS.

An Artificial Intima for Perfusion Apparatus.

V. O. BJÖRK (*The Journal of Thoracic Surgery*, September, 1950) describes a simple method of coating internally the glassware and rubber tubing of perfusion apparatus with a water-repellent substance, in order to diminish friction, foaming and fibrin formation, and to retard the clotting of blood. The substance used is an organic compound of silicon known as "Siloxan UHB 300". An advantage of using apparatus so prepared for perfusion is that it is possible to use smaller and more easily neutralized doses of heparin.

Temporal Arteritis and Aureomycin.

J. M. RICE-OAKLEY and A. M. COOKE (*The Lancet*, January 13, 1950) describe the treatment with aureomycin of two patients suffering from temporal arteritis. One was symptom-free after two weeks' treatment with 0·5 gramme given six-hourly and has remained well since. The other tolerated aureomycin badly and the course was cut short; however, considerable improvement was noted, and relapse occurred within forty-eight hours of withdrawal of aureomycin. Further trial is recommended.

Streptomycin and Tuberculous Lesions of Trachea and Bronchi.

THE Streptomycin in Tuberculosis Trials Committee of the Medical Research Council (*The Lancet*, February 3, 1951) reports a cooperative trial in six hospitals of streptomycin in the treatment of tuberculous tracheobronchitis. In the 35 patients treated, the amount of lung disease varied widely, cavitation being present in 10 cases. In 24 of the 35 patients the bronchial lesion was found to be greatly improved in appearance or healed when the final bronchoscopy was carried out four or six months after the start of treatment. In 15 of 33 patients who underwent bronchoscopy two months after the start of treatment, there was much improvement in the appearance of the bronchial lesions; later relapse was noted in only one case. A satisfactory later response of the bronchial lesion was unusual if some improvement was not found two months after treatment began. Healing of the bronchial lesion was more frequent in patients with limited lung disease than in those with tuberculous cavities. Bronchial stenosis was present before treatment in 15 patients, and in seven more it developed during treatment; the report states that in some cases it may necessitate later surgical treatment. Sputum conversion took place in 24 cases, the patients including two treated by artificial pneumothorax, one treated by thoracoplasty and one treated by pneumonectomy. In two cases, in spite of streptomycin treatment, masses of granulation tissue required removal at repeated bronchoscopy. Some patients received two grammes of streptomycin daily, others received one gramme daily. The report states that the figures are too small to allow a firm conclusion to be drawn from the results; there is only a slight suggestion that the lower dosage was less satisfactory.

Pernicious Anæmia and Citrovorum Factor.

L. S. P. DAVIDSON and R. H. GIRDWOOD (*The Lancet*, March 31, 1951), in a preliminary communication, describe the treatment of three patients suffering from Addison's pernicious anæmia with 20, 40 and 80 biological units respectively of citrovorum factor. The results suggest that, provided a large enough dose is given, the citrovorum factor will produce a hæmatological and clinical response in patients with pernicious anæmia; at least 80 million units were found necessary in this investigation. The authors state that it is certain that the activity of refined liver extract in the treatment of pernicious anæmia is not related to its content of either citrovorum factor or folic acid, which is very small, but to its content of vitamin B_{12}.

Citrovorum Factor and Folic Acid Antagonists.

E. B. SCHOENBACH, E. M. GREENSPAN and J. COLSKY (*The Journal of the American Medical Association*, December 30, 1950) state that two patients who had received amethopterin or aminopterin for treatment of metastatic neoplasm developed leucopenia and ulcerated mouth lesions. They were treated with citrovorum factor, without discontinuation of the daily dose of the folic acid antagonist. The mouth lesions promptly healed and the leucopenia disappeared. The authors consider that the reversal of these toxic manifestations by citrovorum factor may be a distinct clinical aid when the folic acid antagonists are used for the treatment of selected neoplastic states. The authors' observations in experimental animals and their experience with these patients indicate to them that citrovorum factor, in contrast to folic acid, is able not only to prevent but to reverse some of the established toxic manifestations of the potent folic acid antagonists mentioned.

Thiouracil and Paroxysmal Cardiac Arrhythmia.

H. D. RUSKIN (*The Lancet*, January 20, 1951) reports the administration of methyl and/or propyl thiouracil to seven patients with paroxysmal cardiac arrhythmia. He states that in four cases the paroxysms were completely prevented, in two they became less frequent and severe, and in one there was no response. In two cases the combination of a thiouracil compound with quinidine was more effective than either drug alone.

Rheumatoid Arthritis Treated with DOCA and Ascorbic Acid.

WALLACE GRAHAM, T. E. HUNT and DAVID MORVAT (*The Canadian Medical Association Journal*, August, 1950) present the results of treatment of 50 patients suffering from rheumatic diseases, with desoxycorticosterone acetate (DOCA) and ascorbic acid administered parenterally. There were 37 cases of rheumatoid arthritis, 10 cases of ankylosing spondylitis and three cases of acute gouty arthritis in the series. In most of the patients no obvious change, either subjective or objective, was noted. A few patients described a temporary relief from stiffness and pain, especially after the first injection, and sometimes this was dramatic. However, in view of the psychological factors involved, the authors interpreted this with caution. Treatment for periods up to fourteen days was found to have no effect on the activity or the progression of the diseases, as shown by the degree of swelling, the erythrocyte sedimentation rate and the serum protein fractions. The treatment had no effect on the total circulating eosinophile cell counts or on glucose tolerance curves, such as are found after therapy with cortisone or ACTH.

Chloramphenicol and Ocular Infection.

IRVING H. LEOPOLD (*Archives of Ophthalmology*, January, 1951) records the results of clinical experience with chloramphenicol ("Chloromycetin") in the treatment of ocular infections. "Chloromycetin" therapy was used in 103 eyes affected by conjunctivitis, with improvement in 71 eyes. Solution in a strength of 2·5 milligrammes per millilitre was used every ten minutes for six doses, then every thirty minutes for four doses, and then every hour for five doses. Thereafter the drops were used every two hours, and when the conjunctiva had cleared the drug was instilled four times daily for the next forty-eight hours. In the treatment of keratitis the drug was administered systemically as well as locally; the dosage used for systemic therapy was three grammes initially, followed by 0·5 gramme every four hours, and local therapy consisted in instillation of two drops of "Chloromycetin" solution, 2·5 milligrammes per millilitre, at hourly intervals. Ten cases of uveitis were not influenced by the administration of "Chloromycetin", but it was found to lessen the severity of *herpes zoster ophthalmicus*. The drug was also used in intraocular infection and dacryocystitis with good effect in some cases.

NEUROLOGY AND PSYCHIATRY.

Frustrated Ambivalence of the Mating Instinct.

C. E. H. TURNER (*The Journal of Mental Science*, April, 1950) states that the regularity with which patients accept and benefit by being told of the psychosomatic theory of family sexuality in the explanation of their symptoms encourages him to believe that the theory gives a true explanation of a normal incidence of ambivalence. When the patients are helped to reorientate themselves with regard to their ambivalence, the pathological manifestations are neglected in favour of normal ambivalence despite the frustrations of life. Mating according to this theory is portrayed by the conditions of the hunt. The male portrays the hunter, who is aggressive and risks his life; the female is portrayed as the inferior species until the orgasm, when she is identified with the superior species which kills the hunting male. The daily life of the family may be regarded conversely as a sublimation of their sexual emotions. The symptoms of ambivalence denote frustration of the normal ambivalence of sexuality. The author gives an

outline immediately the patient has declared symptoms which can be explained by it, and explains aspects of sexuality which have been misunderstood. The cause of the frustration may require slight or deep analysis.

Shock.

A. M. MEERLOO (*The Journal of Nervous and Mental Disease*, June, 1950) discusses shock as a psychosomatic phenomenon. He regards it as an unadjusted, primitive defence reaction in a traumatic condition, acting in a period of transition to new defensive automatisms. The primary cataleptic defence is shown in the fowl laid on its back. The same type of reactions may be seen in man. In the German concentration camps people went to the slaughter chamber without resistance. The victim of an accident may be as apathetic as the fowl. Referring to surgical shock, the author discusses the psychological implications. He states that the active notion of a disease can paralyse vital functions. When a sufferer from a malignant growth is informed of the diagnosis, this "shock" may have the same effect on him as the fear of death had on a man who was trapped in a bombed air-raid shelter, and who appeared to be completely paralysed by a small superficial wound of his hand. The wound would not heal and for days and days he was in a state of chronic shock, with combined mental and physical symptoms. Shell shock, anxiety neurosis, and combat fatigue are regarded as special examples of the above condition. They are weapons of defence, though at times they may defeat their purpose. It is literally true that a patient can die of fright.

Time Appreciation and Brain Disease.

J. J. COHEEN (*The Journal of Nervous and Mental Disease*, August, 1950) has studied appreciation of time in a group of 69 patients diagnosed as having organic brain disease. The series was controlled by observation on 50 normal subjects. The author finds that varying degrees of agnosia occur in diffuse cortical disease, at least roughly proportional to the degree of deterioration. His method of demonstration is stated to be so simple and easy that it may be used for diagnosis and prognosis.

Attempted Suicide.

DR. WERNER SIMON (*The Journal of Nervous and Mental Disease*, June, 1950) reviews 50 cases of attempted suicide among war veterans (white males). He mentions the common findings of increased frequency on Sundays and of the more frequent but less successful attempts of females. In his series the rate for single men was high (two-thirds). No less than 29 came from broken homes. This tended to produce feelings of insecurity at an early age. Cyclothymic personalities predominated. Schizophrenia headed the list of diagnoses (19), with psychoneurosis second (11). The author quotes Menninger's opinion that alcoholism is a form of partial or chronic self-destruction in connexion with the finding of severe alcoholic addiction in over half of the subjects. The motivation in this series shows a large proportion due to the frustration of readjustment to civilian life (15). A slightly larger number (20) attempted suicide owing to active ideas of persecution or hallucination. Wrist or throat cutting was the commonest method chosen. It is considered that unconscious psychological reactions determine the site of election. That shooting, barbiturate overdose, poisoning and gas are more frequently employed by combat veterans may be due to war experience affecting their sadomasochistic personality components.

Nephrosis After Electroplexy.

L. GOODMAN (*The Journal of Nervous and Mental Disease*, August, 1950) describes two cases in which lower nephron nephrosis followed electroconvulsive therapy. Death occurred in both. It is suggested that the electric current produces factors leading to progressive renal insufficiency; this is in keeping with experimental evidence. The number of shock treatments appears to have no bearing. The onset of diarrhœa may be a pointer to the onset of renal damage.

Adult Court Psychiatric Clinics.

MANFRED S. GUTTMACHER (*The American Journal of Psychiatry*, June, 1950) states that the establishment and general acceptance of adult court psychiatric clinics have been amazingly slow. Those that have been established serve principally criminal courts. The proceeding is somewhat different: in one clinic 90% of the psychiatric examinations are made prior to trial; in another 85% are made after trial but before sentence. There is more to offer than the detection of insanity. Such a clinic should be better able than the law to detect motives, to find guilt-ridden individuals with abnormal needs for punishment, to measure antisocial drives, and also to assess the potentialities of punishment, probation and psychotherapy. The writer, who was an adviser to a committee of the United Nations studying the prevention of crime and the treatment of offenders, advised the establishment of an institute which before a trial would furnish a report stating whether the defendant was competent to stand trial and whether there was any doubt as to his responsibility at the time of the crime. After the trial a full diagnostic and advisory report would be made available based upon the psychiatric, psychological and social worker's reports.

Cardiac Complications in Electroconvulsive Therapy.

A. J. BANKHEAD, J. K. TORRENS and T. H. HARRIS (*The American Journal of Pychiatry*, June, 1950) identify two types of cardiac reaction in electroconvulsive therapy: vagal reactions and ectopic beats. They have found that the first occurred following treatment and was characterized by irregularity and slowing of the pulse, peripheral vascular collapse, prolonged apnœa, excessive salivary and bronchial secretion, and excessive nausea and vomiting. Vagal reactions were recognized in 30% of patients in a series investigated and were alarming in 4%. The second type of abnormality occurred during the deepest post-convulsive cyanosis and was more severe and observed more frequently in patients with heart disease. Transient runs of ventricular tachycardia were considered the most potentially dangerous occurrence. Atropine sulphate (one-thirtieth of a grain given intramuscularly) was considered to be free from danger, and it is advised for patients who have previously had vagal reactions and electrocardiographic evidence of vagotonia. For those with ectopic beats, particularly when of ventricular origin, quinidine sulphate (one one-hundred-and-eleventh grain given four times a day) is recommended. The authors have noted that both these reactions were more frequently observed when multiple stimuli were given before a convulsive response was obtained. Their investigations were prompted by two deaths occurring immediately after treatment, in which autopsy findings failed to establish a definite cause of death.

Memory and Electroconvulsive Therapy.

IRVING L. JANIS (*The Journal of Nervous and Mental Disease*, May, 1950) has studied the duration of amnesia after electroconvulsive therapy. He found that it was present in his entire series (19) four weeks after termination of treatment. Some amnesia was present after two and a half to three and a half months. It was noted that some failures were quite temporary and could be easily overcome.

Elective Mutism in Children.

D. J. SALFIELD (*The Journal of Mental Science*, October, 1950) describes a rare form of mutism, unassociated with signs indicating a lesion of the nervous system, the sensory apparatus, or the organs of articulation and phonation. He states that the intellectual level does not explain the mutism, and it appears that the crucial factor is emotional. Elective mutism is understood to mean an unwillingness to make the effort of speaking under certain conditions. Shyness combined with speech blocking in the presence of strangers, especially adults, is a normal early infantile trait. As an exaggerated form of this reaction a pathological fixation of this kind may come about. In the present case, there was hereditary tainting and a sensitive, not defective, child with an insecure home background.

Mild Manic Depressive Psychosis.

JOHN D. CAMPBELL (*The Journal of Nervous and Mental Disease*, September, 1950) has taken a group of 1000 manic-depressive patients and excluded those whose depression might have been of reactive type or who were in the fourth or fifth decade of life. The records of the residue (200) were collated and form a group of mild manic-depressives. The author states that a wide variety of symptoms is involved. There is a galaxy of psychosomatic symptoms. The emotional disturbances are numerous. Anxiety is prominent and "free-wheels" to anything. The results are worries, fears, phobias or preoccupation with physical symptoms. There is a lesser involvement of the mental processes. The author stresses the fact that the number of mild depressives in the community is legion, and many are wrongly treated for some medical or surgical disease. He quotes illustrative cases and discusses the differential diagnosis. He pleads for more research in this condition.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal Alexandra Hospital for Children, Camperdown, on April 18, 1951. The meeting took the form of a series of clinical demonstrations by members of the honorary medical and surgical staffs of the hospital.

Tuberculous Meningitis.

DR. D. G. R. VICKERY showed three patients who were being treated for tuberculous meningitis.

When the first child, a boy, aged six months, was admitted to hospital, his father was in hospital with "open" tuberculosis. On September 3, 1950, the mother had begun to notice that the child was fat around the neck owing to lumps under both sides of the jaw. There was no history of sore throat. By October 27 the lumps were slightly bigger. The baby had been quite well, had been eating and gaining weight, was active and had no cough. On examination he was found to have a temperature of 98·4° F. There were large, hard, rounded cervical glands fixed to deeper structures in both posterior triangles. The spleen was palpable. There were no other abnormal physical signs. The result of a Mantoux test was positive at a dilution of 1:1000. The blood sedimentation rate was 16 millimetres per hour. The red blood cells numbered 3,900,000 per cubic millimetre. The hæmoglobin value was 10·4 grammes *per centum*. The colour index was 0·88. The leucocytes numbered 12,500 per cubic millimetre, made up of neutrophile cells 39%, lymphocytes 45%, monocytes 15% and eosinophile cells 1%. A growth of *Mycobacterium tuberculosis* was obtained after six weeks' incubation of material obtained by gastric lavage. X-ray examination of the chest revealed numerous small partly calcified nodules with a fine nodular mottling in both lungs. No definite evidence of active tuberculosis could be seen. On January 28, 1951, the child's temperature was 99·4° F., but there was no other sign of infection. The cerebro-spinal fluid contained 150 leucocytes per cubic millimetre, made up of mononuclear cells 95% and polymorphonuclear cells 5%; the protein content was 20 milligrammes *per centum* and the chloride content 730 milligrammes *per centum*; the result of the test for sugar was positive; no organisms were seen on examination of a smear. The treatment being given was the administration of streptomycin 50 milligrammes once a day by the intrathecal route for five weeks and 200 milligrammes twice a day by the intramuscular route, the latter being continued. In addition PAS was being given in a dosage of one-half gramme four times a day.

The second patient was a girl, aged ten years. The history was that whilst pregnant with this child in 1940, the mother had been discovered to have pulmonary tuberculosis. After parturition her condition had deteriorated fairly rapidly, but she continued to look after the child until late in 1941 when she entered an institution, where she died in 1943. The child had been in a sanatorium from February, 1947, to September, 1947, under treatment for pulmonary tuberculosis. The present illness had commenced on November 23, 1950, when the child began to lose her appetite and become irritable. Two weeks later she had a sudden fainting attack with severe frontal headache, which lasted only a short time. Next day she vomited. Two days later the vomiting recurred, and the child was drowsy and delirious with complete anorexia. On examination of the child on December 16 her temperature was 100·4° F. She was comatose but in no distress. There was slight but definite neck stiffness. Kernig's sign was present. There were no other abnormal physical signs. The cerebro-spinal fluid contained 220 leucocytes per cubic millimetre, made up of polymorphonuclear cells 10% and lymphocytes 90%; the protein content was 70 milligrammes *per centum* and the chloride content 700 milligrammes *per centum*; the result of the test for sugar was positive. The result of a Mantoux test was positive for a dilution of 1:1000. The blood sedimentation rate was four millimetres per hour. X-ray examination of the chest revealed scattered irregular consolidation in the upper halves of both lungs, the appearance being suggestive of the adult type of tuberculosis; there was a healed primary tuberculous complex at the base of the left lung. Streptomycin had been given by the intrathecal route, 50 milligrammes per day, for one month, and was being continued by the intramuscular route, 750 milligrammes twice a day. PAS, three grammes on six days a week, was also being given.

The third patient, a girl, aged seven years, had a past history of measles, but no history of contact with tuberculosis. On September 23, 1950, she had become tired and listless, with vomiting and diarrhœa. Examination of the child revealed a slight temperature rise with slight abdominal tenderness. On September 28 the child became drowsy and listless and lost her appetite. Her temperature was 102° F., but no other abnormality was noted. On October 2 the drowsiness was still present. The child was irritable on being disturbed and she complained of pain in the neck and back. On October 3 she was admitted to hospital. Her temperature was 99·4° F. She was drowsy and irritable and had a dry tongue. There was slight neck and back stiffness. Kernig's sign was present. All tendon reflexes were exaggerated. The abdominal reflexes were present, and the plantar reflexes were flexor in type. There were no other abnormal physical signs. The cells in the cerebro-spinal fluid were monocytes 95% and polymorphonuclear cells 5%; the protein content was 100 milligrammes *per centum* and the chloride content 600 milligrammes *per centum*; the result of the test for glucose was negative; acid-fast bacilli were present in a smear. Material obtained by gastric lavage had been incubated, but the results were not yet to hand. The lungs appeared normal to X-ray examination. The result of a Mantoux test was positive in a dilution of 1:1000. A blood count revealed a total of 4,500,000 erythrocytes per cubic millimetre, a hæmoglobin value of 12·0 grammes *per centum*, a colour index of 0·89 and a total of 20,300 leucocytes per cubic millimetre. Treatment consisted of streptomycin, which had been given intrathecally in a dosage of 50 milligrammes daily for twenty-eight days and then 50 milligrammes every second day for twenty-eight days, and was still being given intramuscularly in a dosage of one-half gramme twice a day. In addition PAS was being given in a dosage of 1·5 grammes every six hours.

Acute Lymphatic Leuchæmia.

DR. S. G. BRADFIELD presented a boy, aged three years, who had been admitted to hospital on February 22, 1951. Three weeks previously the child's mother had noticed that he was not well; he was irritable and bruised easily. After a week he developed swollen glands in the neck, for which sulphadiazine was prescribed by the local doctor. Next day a blotchy rash appeared on his arms and that had since spread. Four days before his admission to hospital, the left testicle commenced to swell and that had become worse. About 10 tablets of sulphadiazine had been given in all. Examination of the child revealed that he had a pale waxy skin with pallor of mucous membranes, numerous bruises and one purpuric lesion, enlarged cervical, axillary inguinal and epitrochlear glands, an enlarged liver and an enlarged spleen, a swollen left testicle, a blotchy rash on exposed parts of the skin, enlarged and infected tonsils and a systolic mitral murmur in the heart. A blood transfusion was given soon after the child's admission to hospital because of severe anæmia. That did little to improve his condition, and the site on which they had cut down to start the transfusion became rapidly and severely infected; the infection did not respond to penicillin therapy. A blood count suggested a diagnosis of acute lymphatic leuchæmia, and that was later substantiated by marrow biopsy. Professor L. F. Dods was called into consultation and advised the trial of α-methopterin in dosage of 2·5 milligrammes for three days, then 5·0 milligrammes daily. This therapy was carried out and resulted in a pronounced remission. The blood count rapidly returned to normal, the liver regressed in size, and the child appeared considerably improved. He was discharged from hospital to his home on March 28 and was still under treatment with α-methopterin and having repeated blood counts.

Miliary Tuberculosis with Meningitis.

Dr. Bradfield's second patient, a girl, aged two and a half years, had been admitted to hospital on December 6, 1950, with a history of developing measles three weeks before; the rash had been present for a week, disappeared for a day and then reappeared for a further week. The child's condition had not improved and she was noticed to have grunting respirations for the last week, becoming much worse for the last day. She had a slight cough, was drowsy and feverish and had been vomiting for two days. Her urine had been dark on and off since she had become ill. She had been given penicillin and sulphadiazine for four days without response. Investigation of the family history revealed no tuberculosis of immediate relatives. However, the mother's cousin, who lived next door, had extensive bilateral pulmonary tuberculosis with tuberculous laryngitis and demonstrable organisms in the sputum, and

another cousin, who also had lived next door recently, had developed pulmonary tuberculosis with collapsed lung. Examination of the child at the time of admission to hospital revealed grunting respirations and diminished percussion note, diminished breath sounds and a few crepitations at the right lung base. No neck stiffness or Kernig's sign was detected, but there was a tendency to "flappy" right hands. Reflexes were all present and normal. The abdomen was soft and without palpable masses, tenderness or guarding; the spleen was not palpable. A blood count revealed that the erythrocytes numbered 4,440,000 per cubic millimetre; the hæmoglobin value was 10·6 grammes *per centum* and the colour index 0·80; the leucocytes numbered 19,300 per cubic millimetre, made up of neutrophile cells 67%, lymphocytes 19%, monocytes 13% and eosinophile cells 1%. Chest X-ray examination revealed generalized nodularity and an enlarged right hilus, the appearance being consistent with miliary tuberculosis; the heart did not appear "mitralized". The Mantoux response was negative with a dilution of 1:1000 and positive with a dilution of 1:100. Examination of material obtained by gastric lavage revealed numerous acid-fast bacilli morphologically resembling *Mycobacterium tuberculosis*, and culture produced a moderate growth of *Mycobacterium tuberculosis* after five weeks' incubation. The cerebro-spinal fluid was clear with flecks; it contained 451 leucocytes per cubic millimetre, made up of mononuclear cells 60% and polymorphonuclear cells 40%, with an occasional red blood cell; the total protein content was 70 milligrammes per 100 millilitres and the total chloride content 680 milligrammes per 100 millilitres; the result of the test for glucose was negative. For treatment the child had been having 350 milligrammes of streptomycin intramuscularly twice a day since December 7, 1950, and that was still being given. Fifty milligrammes of streptomycin had been given intrathecally daily for twenty-eight days from December 8, 1950, and another course with the same dosage started on February 26, 1951, and was still being carried out. The child had also been having PAS one gramme by mouth eight-hourly since January 4, 1951.

Subacute Liver Atrophy.

Dr. Bradfield finally showed a girl who had been admitted to hospital on January 1, 1951. Three other children in the family had contracted jaundice, and on November 1, 1950, the patient's mother had noticed that the patient's urine was very dark. Soon afterwards she had become jaundiced and lost her appetite. Recovery had commenced in about a week, the jaundice had faded, and the urine had become normal in colour. On December 1 the child had developed diarrhœa, and her stools had again become clay-coloured and the jaundice had reappeared. From December 10 onwards she had been in bed and had lost much weight. For several days before her admission to hospital she had been drowsy all day, but had become very restless at night. On the day of her admission to hospital she was almost comatose and could be roused only with difficulty. She was found on examination to be a comatose extremely ill child, very deeply jaundiced. All reflexes were absent. The chest was apparently normal. Bradycardia was present, but the heart was not enlarged, and no murmurs were audible. Liver dulness was much decreased, but there was no ascites and the spleen was not palpable. Intravenous administration of fluids was commenced at once together with polyvitamin therapy. For about one week the child's condition improved slowly, then suddenly relapsed. Death appeared imminent during the next five days, but then again she began to improve slowly. On January 18 she was much brighter, playing and talking; the fæces contained bile. Thenceforward the jaundice faded slowly and the irritability decreased. By February 22 the child was considered cured and was sent to Collaroy to convalesce.

Epilepsy.

DR. D. G. HAMILTON showed a boy, aged two years and ten months, who had had major epileptiform seizures each few weeks since the age of eleven months. There was no history of cerebral birth injury, and the boy's general development had been satisfactory. His mother had had a convulsion at the age of eleven months. His electroencephalogram showed a mixture of very fast and very slow activity—an abnormal record consistent with a diagnosis of epilepsy. His fits were partly controlled by phenobarbital, but had been completely controlled by the administration three times a day of a combination of phenobarbital, one-quarter of a grain, and "Dilantin", one-half of a grain. Dr. Hamilton said that the interest of the case lay in the association between epilepsy in the child and an infantile convulsion in the mother. An association between those two conditions was frequently seen; for example, an infant might have several febrile convulsions and later in childhood have epileptic fits of any type, or one member of a family might have undoubted epilepsy and another have an occasional febrile convulsion. There was a good deal of evidence to support the view that those were but different degrees of the same disease, idiopathic epilepsy. If a child had febrile convulsions, any of the following criteria warranted a provisional diagnosis of epilepsy and the continued use of anticonvulsants till the child had been free of fits for at least a year: (i) the first convulsion before the age of one year; (ii) severe, prolonged or frequent convulsions; (iii) a convulsion without an obvious precipitating cause; (iv) a family history of epilepsy; (v) an abnormal electroencephalogram.

Dr. Hamilton's second patient was a girl, aged seven years, who for one year had had typical frequent *petit mal* fits. Dr. Hamilton said that they could be produced by over-breathing, as was not uncommon in *petit mal*. The past and family history was clear of evidence of epilepsy or brain damage. The electroencephalogram showed runs of three cycles per second with spikes and waves typical of *petit mal*. Phenobarbital caused no improvement and made her irritable, as it fairly often did. "Tridione" greatly reduced the number of fits, but even with a dosage of five capsules daily, each of 0·3 gramme, she still had some fits. "Prominal" and "Dexedrine" had been tried without benefit. Dr. Hamilton explained that sometimes *petit mal* was readily controlled by phenobarbital or "Prominal". If those failed "Tridione" should be used; it dramatically stopped the fits in some cases, reduced them in some, but in some failed utterly to influence them. It could cause photophobia, skin rashes and depression of all the formed elements of the blood, affecting the neutrophile leucocytes first; a blood count should be carried out each month while a patient was taking the drug, distinct neutropenia being an indication for stopping its administration at once.

The next patient, a boy, aged three years, had had his first major epileptiform convulsion at the age of ten months while teething. At the age of eighteen months he had commenced to have frequent akinetic fits, suddenly dropping forward and immediately recovering; that happened several times every day. Since that time he had had occasional major and very frequent akinetic fits. They might happen many times a day, and the child had repeatedly bruised or cut his face during them. His family and previous history was normal, but his electroencephalogram was grossly abnormal, consisting of continuous slow wave and spike discharges. Treatment had been started with phenobarbital and "Dilantin". No major fits occurred while he was having those drugs, but many akinetic fits did. The "Dilantin" was replaced by "Tridione". Akinetic fits continued, and the dosage of phenobarbital was gradually increased to one grain four times daily and "Tridione" 0·3 gramme six times daily, but without any impressive benefit. Then the child's total white cell count fell to 2600 per cubic millimetre with only 806 or 31% neutrophile cells, and submucous hæmorrhages appeared in the gums and impetigo on the face. The "Tridione" therapy was immediately stopped, and the boy was admitted to hospital. Fortunately he recovered from the toxic effect of "Tridione" without any special treatment. The dreaded pancytopenia with a fulminating illness characterized by bleeding, uncontrolled hæmorrhage and anæmia was very narrowly averted. Recently the boy had had "Prominal" one grain three times a day with phenobarbital one grain three times a day. With these drugs he had been much better, having a few akinetic fits and a few mild major ones; because of the latter, "Dilantin" half a grain four times daily had been added. Dr. Hamilton said that the case demonstrated the failure of "Tridione" to control one of the *petit mal* triad with a spike and wave tracing and the serious danger of large doses of "Tridione". "Prominal" was probably proving of much greater benefit to the patient and was a most useful general purpose drug in epilepsy.

The fourth patient, a girl, aged six years, had for two years had major epileptiform fits and for one year *petit mal* turns. A maternal aunt was an epileptic. The electroencephalogram showed runs of high voltage very fast spikes. Phenobarbital one-quarter of a grain three times a day prevented major fits, but *petit mal* turns continued to occur two to three times a day. For the last month "Tridione" 0·3 gramme twice a day had been added to the phenobarbital, and both major and minor fits had been controlled.

Dr. Hamilton then showed a girl, aged eighteen months, who had suffered cerebral injury at birth. The delivery was normal, but the liquor was heavily stained with meconium. The baby was slow to breathe, and for some days was

irritable and inclined to vomit, and there was some spasm of the left arm. Oxygen was required for several days to prevent cyanosis, and the baby was then lethargic for two weeks. For the last six months the baby had had minor motor fits on several occasions. She fell over, became blue around the mouth, and was then pale and unconscious and limp for about a minute. There was no twitching. After the turn she slept for an hour. The electroencephalogram record was normal. There were now no neurological signs of the cerebral birth injury, and the child's general progress had been good. Phenobarbital had failed to control the fits and "Dilantin" was now being given as well.

Dr. Hamilton's next patient, a boy, aged nine years, had been born from a persistent occipito-posterior position after a labour of forty-eight hours' duration and had been very ill for the first two weeks of life. The mother also had had rubella in the fourth month of pregnancy, and the boy was deaf to high frequencies, probably because of the rubella. For two years he had had major epileptiform fits, as well as two distinct types of brief minor motor turns, in which he turned his head, grunted and tried to say "turn", or bent forward and threw out his hands. The electroencephalogram suggested left-sided brain damage; the pneumoencephalogram showed no definite abnormality. His mental age was retarded two years, but there were no physical signs of localized brain injury. Phenobarbital and "Dilantin" controlled the major fits, but he was having many of the minor turns (as many as 50 in a month). Dr. Hamilton said that they were trying the effect of "Tridione" and "Prominal" at present. "Tridione" would probably not be of value, for the fits resembled minor motor ones rather than *petit mal* fits. However, the distinction was not always easy to make, and if one anticonvulsant failed it was worth while to try another. If a drug showed any promise of helping, its dose should be pushed to the limit of tolerance if fits were still not controlled. If it still failed, another drug should be tried. Children with a variety of fits resulting from organic brain damage were among the most difficult to treat.

The last patient in Dr. Hamilton's series, a boy, aged eight years, had been taking phenobarbital and "Dilantin" for two years for major epilepsy, with good control of the fits. The dose of "Dilantin" had been half a grain three times a day at first, and then had been reduced to half a grain twice a day six months before. He now had hypertrophy of the gums, which was, Dr. Hamilton said, a typical slowly developing toxic effect of "Dilantin". The other toxic effects of "Dilantin" were ataxia and drowsiness, which appeared promptly if too big a dose was given, and a rash, which might appear at any time, but was most likely soon after the drug was first given.

Pink Disease.

Dr. Hamilton with DR. C. W. G. LEE presented the results of biochemical and hæmatological investigations of children suffering from pink disease who had and had not been given salt in addition to their diet. There was no evidence of alteration in plasma sodium, chloride or protein content, but in most cases there was hæmoconcentration. Administration of three to nine grammes of salt per day for many weeks caused no alteration to the figures obtained. These results were published in detail in this journal in the issue of April 14, 1951, at page 565.

(*To be continued.*)

The Royal Australasian College of Physicians.

ALLOCATION OF SUPPLIES OF CORTISONE.

THE executive committee of The Royal Australasian College of Physicians in considering applications for supplies of cortisone and in authorizing its allocation will observe the following principles:

1. Preference in allocation will be given to those hospitals or institutions which are carrying out investigational work under the supervision of a committee specially appointed for this purpose. Applications for supplies of cortisone for use within such hospitals should therefore be made through the committee so appointed and this committee will be requested to supply full reports of the investigational work undertaken with complete case histories.

2. Applications from individual practitioners for supplies of cortisone for use in a particular case in a private hospital or a research project will be considered by the executive committee provided that the following details are given: (*a*) Essential clinical data of each case or projected research. (*b*) The estimate of the amount of the drug required. (*c*) Details of where the treatment is to be carried out. (*d*) An undertaking to supply a full report of results of treatment in each particular case, including the following investigations: (i) blood count, including hæmoglobin estimation and eosinophile cell count; (ii) erythrocyte sedimentation rate; (iii) X-ray examination of bones and joints (if applicable); (iv) presence of signs of cardiac and/or renal disease, tuberculosis and *diabetes mellitus*; (v) where available, electrocardiogram, blood potassium and urinary steroid levels.

3. As supplies of cortisone are still limited, the executive committee will only consider applications for its use in the treatment of the following diseases: (*a*) acute rheumatic fever with carditis; (*b*) rheumatoid arthritis with florid and reversible manifestations, particularly in patients in the younger age and wage-earning groups; (*c*) Still's disease; (*d*) Addison's disease; (*e*) *status asthmaticus*, if life is endangered; (*f*) acute disseminated *lupus erythematosus*; (*g*) exfoliative dermatitis (severe); (*h*) drug reaction, if life is endangered; (*i*) pemphigus (severe), if life is endangered; (*j*) acute inflammatory eye diseases, if sight is endangered.

4. The quantity of the hormone required should be stated by the applicant, who should have familiarized himself with the published literature before attempting treatment.

5. The College in granting an allocation of cortisone does not accept any responsibility for its use, which remains with the medical attendant alone.

6. All applications, either for an allocation of the hormone already imported or for a licence to import direct from the manufacturers, should be forwarded to the Honorary Secretary of The Royal Australasian College of Physicians, 145 Macquarie Street, Sydney. If, however, an allocation is required for an acute emergency, application should be made direct to one of the following:

Queensland.—Dr. Alex Murphy, Ballow Chambers, Wickham Terrace, Brisbane. Telephone: B 0811; after hours, M 1710. Dr. Otto Hirschfeld, Ballow Chambers, Wickham Terrace, Brisbane. Telephone: B 8657; after hours, M 1086.

New South Wales.—The Royal Australasian College of Physicians, 145 Macquarie Street, Sydney. Telephone: BU 3288; after hours, UA 1761 or XY 2137,

Victoria.—Dr. Ewen Downie, 111 Collins Street, Melbourne. Telephone: JM 1440; after hours, BJ 2061. Dr. G. A. Penington, 61 Collins Street, Melbourne. Telephone: FA 8583; after hours, WJ 1220.

South Australia.—Dr. K. S. Hetzel, 163 North Terrace, Adelaide. Telephone: Central 3193; after hours, F 3403. Dr. Guy Lendon, 21 King William Street, Adelaide. Telephone: Central 248; after hours, M 9893.

Western Australia.—Dr. Cyril Fortune, 244 St. George's Terrace, Perth. Telephone: B 4835; after hours, Scarborough 72. Dr. James Young, 131 Scarborough Beach Road, Mt. Hawthorn, Perth. Telephone: B 5760.

Tasmania.—Dr. Ralph Whishaw, 174 Macquarie Street, Hobart. Telephone: Hobart 6604; after hours, Hobart 9032. Dr. G. A. Robbie, Royal Hobart Hospital, Hobart. Telephone: Hobart 5091.

SIMS COMMONWEALTH TRAVELLING PROFESSOR, 1951.

DR. D. M. DUNLOP, B.A. (Oxon.), M.D. (Edin.), F.R.S. (Edin.), F.R.C.P. (Edin.), who is visiting Australia and New Zealand as the Sims Commonwealth Travelling Professor for 1951, will deliver lectures in all States of the Commonwealth during the period June to August, 1951, beginning in Brisbane and Sydney. The lectures will be open to all members of the medical profession.

The lectures in Brisbane will be delivered in the Main Lecture Theatre, Medical School, Herston, at 8.30 p.m., on the following dates: Tuesday, June 5, "The Effect of the Endocrine Glands on the Skin". Thursday, June 7, "Changing Fashions in Medicine". Friday, June 8, "Some Medical Aspects of Obstetrics and Gynæcology".

The lectures in Sydney will be delivered in the Stawell Hall of The Royal Australasian College of Physicians, 145 Macquarie Street, Sydney, at 8.30 p.m., on the following

dates: Friday, June 15, "The Effect of the Endocrine Glands on the Skin". Wednesday, June 27, "Changing Fashions in Medicine". Wednesday, July 4, "Some Medical Aspects of Obstetrics and Gynæcology".

WUNDERLY TRAVELLING SCHOLARSHIPS.

THE Royal Australasian College of Physicians proposes to award two Wunderly Travelling Scholarships in 1952 for the post-graduate education and training abroad of young physicians in the diagnosis and management of thoracic disease. The value of each scholarship is £1000 Australian currency. The scholarships will be tenable by graduates in medicine of a university approved by the College, who hold a doctorate of medicine and/or a Fellowship or Membership of The Royal Australasian College of Physicians or of the Royal College of Physicians of London, but the holding of a higher degree or diploma is not an absolute condition of the award.

Information relating to the scholarships may be obtained upon application to the Honorary Secretary of the College at 145 Macquarie Street, Sydney.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that on Thursday, June 28, Dr. R. J. Walsh and Dr. H. O. Lancaster will present a paper entitled "The Accuracy of Routine Hæmatological Methods (Other than Counting)" to the Statistical Society of New South Wales at the School of Public Health and Tropical Medicine at 7.30 p.m. All visitors are welcome.

Congresses.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE (1952).

AN international congress of physical medicine, organized by the British Board of Management of the International Federation of Physical Medicine, will be held in London from July 14 to 19, 1952. The President will be Lord Horder, the Vice-Presidents Dr. Frank Howitt, Dr. Philippe Bauwens and Dr. Frank S. Cooksey, and the Honorary Secretary, Dr. A. C. Boyle.

In accordance with the regulations of the International Federation of Physical Medicine, the meetings of the congress will be reserved for matters dealing with the clinical, remedial, prophylactic and educational aspects of physical medicine and with the diagnostic and therapeutic methods employed in physical medicine and rehabilitation. Technical, scientific and historical exhibitions also will be arranged.

Applications for the provisional programme should be addressed to the Honorary Secretary, International Congress of Physical Medicine (1952), 45 Lincoln's Inn Fields, London, W.C.2.

Obituary.

RUPERT WALTER HORNABROOK.

WE regret to announce the death of Dr. Rupert Walter Hornabrook, which occurred on May 7, 1951, at Toorak, Victoria.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED APRIL 28, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	*	..	..	..	..	..	..	..	..
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	2(1)	..	1	..	..	..	..	..	3
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	1(1)	..	1(1)	..	..	..	2
Diphtheria	11(1)	5(3)	3(1)	1(1)	3(2)	..	..	..	23
Dysentery (Amœbic)	*	1(1)	..	..	..	..	..	..	1
Dysentery (Bacillary)	*	..	3(3)	..	1	..	..	2	6
Encephalitis Lethargica	..	4(2)	..	..	..	..	..	..	4
Erysipelas	*	*	*	1(1)	*	*	..	..	1
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	*	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	1(1)	..	..	1	..	..	..	2
Measles	*	*	*	15(2)	*	*	..	..	15
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	38(18)	9(2)	22(10)	12(6)	..	1	..	..	82
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	1(1)	..	..	..	..	..	..	..	1
Rubella(*c*)	*	*	..	*	..	*	..	..	..
Scarlet Fever	18(5)	30(21)	3(2)	5(1)	8(4)	2(1)	..	..	66
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	..	*	*	*	*	*	..
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	36(21)	36(29)	7(7)	5(3)	9(7)	1(1)	..	..	94
Typhoid Fever(*e*)	..	..	..	..	..	1	..	..	1
Typhus (Endemic)(*f*)	..	..	..	1(1)	..	..	..	..	1
Undulant Fever	..	..	..	..	..	..	..	..	..
Weil's Disease(*g*)	*	*	2	*	*	*	*	*	2
Whooping Cough	*	*	*	4(4)	*	*	..	..	4
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory.
* Not notifiable.
(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Australian Medical Board Proceedings.

TASMANIA.

THE undermentioned has been registered, pursuant to the provisions of the *Medical Act*, 1918, Tasmania, as a duly qualified medical practitioner:

Belcher, Alan Robert, M.B., B.S., 1950 (Univ. of Melbourne), Rosebery.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Knispel, Marie June, M.B., B.S., 1951 (Univ. Sydney), Balmain and District Hospital, Balmain.

Lester, Vincent, registered in accordance with the provisions of Section 17 (1) (c) of the *Medical Practitioners Act*, 1938-1945, 17 Harriette Street, Neutral Bay.

Mayne, Robert John Bruce, M.B., B.S., 1951 (Univ. Sydney), 22 Bent Street, Lindfield.

Deakin, Malcolm James, M.B., B.S., 1951 (Univ. Sydney), 391 Military Road, Mosman.

Tidswell, Thomas, M.B., B.S., 1951 (Univ. Sydney), Berrima District Hospital, Bowral, New South Wales.

Korner, Paul Ivan, M.B., B.S., 1951 (Univ. Sydney), 3 Hunter Street, Woolwich.

Larum, Cornelius Lloyd, M.B., B.S., 1950 (Univ. Sydney), St. Joseph's Hospital, Auburn.

The undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

Anderson, Hugh Cairns, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Wellington.

Armstrong, John Beresford, M.B., B.S., 1947 (Univ. Sydney), 5 Oswin Street, Parkes.

Atkinson, Kenneth John James, M.B., B,S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Boughton, Clement Russell, M.B., B.S., 1950 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Brassil, Joseph Alexis Carlin, M.B., B.S., 1951 (Univ. Sydney), St. Joseph's Hospital, Auburn.

Cooke, Kenneth Henry Stephen, M.B., B.S., 1951 (Univ. Sydney), 26 Dunmore Street, Bexley.

Doutreband, Allan Roy, M.B., B.S., 1951 (Univ. Sydney), 5 Culdees Road, Burwood.

Gunton, Peter Elliot, M.B., B.S., 1951 (Univ. Sydney), Ryde District Soldiers' Memorial Hospital, Eastwood.

Harrington, Jeffery Gould, M.B., B.S., 1951 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.

Knox, Eleanor Charis, M.B., B.S., 1951 (Univ. Sydney), Rachel Forster Hospital for Women and Children, Redfern.

Lake, Bernard Joel, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Learoyd, Harry Meldrum, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Leckie, Bruce Douglas, M.B., B.S., 1950 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

McKinnon, Donald James, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Pullen, Peter David, M.B., B.S., 1951 (Univ. Sydney), Ryde District Soldiers' Memorial Hospital, Eastwood.

Rogers, James Stewart, M.B., B.S., 1951 (Univ. Sydney), Mater Misericordiæ Hospital, Crows Nest.

Tweedale, Kenneth, M.B., B.S., 1951 (Univ. Sydney), 5 Dowel Street, Chatswood.

The undermentioned have been elected members of the South Australian Branch of the British Medical Association:

Calder, Shirley, M.B., B.S., 1950 (Univ. Adelaide), Eden Hills.

Robinson, Donald Neil, M.B., B.S., 1948 (Univ. Adelaide), c.o. National Bank, Unley Road, Unley, South Australia.

Brandstater, Bernard John, M.B., B.S., 1950 (Univ. Adelaide), 58 Porter Street, Parkside.

Dewar, Colin Chudleigh, M.B., B.S., 1949 (Univ. Adelaide), 43 Elmo Avenue, Unley Park, South Australia.

Heitmann, Dorothea Smith, M.B., B.S., 1949 (Univ. Adelaide), 218 Henley Beach Road, Torrensville, South Australia.

Prest, Elizabeth Maurine, M.B., B.S., 1951 (Univ. Adelaide), 283 Wakefield Street, Adelaide.

Medical Appointments.

Dr. R. A. Isenstein has been appointed as honorary surgeon to the Sterility Clinic of the Royal Adelaide Hospital.

Dr. P. L. Grogan has been appointed Public Vaccinator for the City of Richmond, Victoria.

Dr. V. E. M. Sheppard has been appointed to the Department of Public Health, New South Wales.

Dr. B. G. Clarke has been appointed Acting Government Medical Officer at Cairns, Queensland.

Dr. C. J. Cummins has been appointed to the Department of Public Health, New South Wales.

Dr. N. P. Wilson has been appointed a member of the Chiropody Board of South Australia.

Diary for the Month.

MAY 31.—New South Wales Branch, B.M.A.: Branch Meeting.
MAY 31.—South Australian Branch, B.M.A.: Branch Meeting.
JUNE 1.—Queensland Branch, B.M.A.: Branch Meeting.
JUNE 5.—New South Wales Branch, B.M.A.: Organization and Science Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £4 *per annum* within Australia and the British Commonwealth of Nations, and £5 *per annum* within America and foreign countries, payable in advance.